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# Chinese patent medicines and allergic rhinitis: a protocol of systematic review and meta-analysis based on the 2020 Pharmacopoeia

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## ADMINISTRATIVE INFORMATION

**Support -** Mechanism Research on the Constitution Adjustment Effects of Tuomin Zhiti Decoction in the Prevention and Treatment of Allergic Rhinitis.(GZY-KJS-2024-02).

**Review Stage at time of this submission -** Formal screening of search results against eligibility criteria.

**Conflicts of interest -** None declared.

**INPLASY registration number:** INPLASY202450121

**Amendments -** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 May 2024 and was last updated on 26 May 2024.

## INTRODUCTION

**Review question / Objective** This systematic review and meta-analysis examines the effectiveness and safety of Traditional Chinese Patent Medicines (TCPMs) for allergic rhinitis (AR) as specified in the 2020 Chinese Pharmacopoeia (ChP 2020). The review addresses three key questions: Comparative effectiveness: How does the effectiveness of TCMPs listed in the ChP 2020 compare to western medicine, placebos, or no treatment in the management of AR symptoms? Combination therapy: Do TCPMs offer additive or synergistic benefits when used alongside Western medical treatments for AR? Evidence quality: Using GRADE assessment, what is the overall certainty and quality of evidence supporting the effectiveness and safety of TCPMs for AR?

**Rationale** Traditional Chinese medicine has a long history, and throughout its development, many types of Chinese patent medicines for AR have evolved. Many of these have been included in the Chinese Pharmacopoeia, yet these included medicines have not undergone systematic evaluation. By thoroughly evaluating the existing evidence and acknowledging its limitations, this review will provide valuable insights that could influence clinical practice and future research on TCMPs for AR, potentially leading to improved patient care.

**Condition being studied** Allergic rhinitis, frequently referred to as hay fever, is a widespread chronic condition characterized by inflammation of the nasal lining. This inflammation is a result of the body's immune system overreacting to typically harmless substances like pollen, dust mites, or animal dander. This reaction leads to the release of inflammatory chemicals, causing a range of uncomfortable symptoms. These symptoms commonly include nasal congestion, runny nose, sneezing fits, itchy eyes and nose, postnasal drip,

and headaches. While not usually life-threatening, allergic rhinitis can significantly impair a person's daily life, affecting their sleep, ability to focus, and overall well-being. In more severe cases, it can even contribute to complications such as sinus or ear infections.

## METHODS

**Search strategy** A comprehensive search strategy will be employed to identify all relevant studies using a combination of free-text terms and controlled vocabulary. The PubMed search strategy is as follows: "(tongqiaobiyan"[Title/Abstract] OR "tongqiao biyan"[Title/Abstract] OR "tong qiao bi yan"[Title/Abstract] OR "xinqin"[Title/Abstract] OR "xin qin"[Title/Abstract] OR "xinyibiyan"[Title/Abstract] OR "xinyi biyan"[Title/Abstract] OR "xin yi bi yan"[Title/Abstract] OR "biyankang"[Title/Abstract] OR "bi yan kang"[Title/Abstract] OR "biyankang"[Title/Abstract]) AND ("Rhinitis, Allergic"[Mesh] OR "Rhinitis, Allergic, Perennial"[Mesh] OR "Rhinitis, Allergic, Seasonal"[Mesh] OR "Allergic rhiniti*"[Title/Abstract] OR "Nasal allerg*"[Title/Abstract] OR "Nose allerg*"[Title/Abstract] OR "Pollen allerg*"[Title/Abstract] OR Pollinosis[Title/Abstract] OR Pollinoses[Title/Abstract] OR "Hay fever"[Title/Abstract] OR hayfever[Title/Abstract] OR AR[Title/Abstract]) AND ("Randomized Controlled Trials as Topic"[Mesh] OR "Randomized Controlled Trial"[Publication Type] OR "Controlled Clinical Trial"[Publication Type] OR random*[Title/Abstract] OR placebo[Title/Abstract] OR trial*[Title/Abstract] OR group*[Title/Abstract])".

**Participant or population** This review will consider studies enrolling participants of all ages with a confirmed diagnosis about AR. Diagnosis should according to recognized clinical criteria or guidelines, encompassing both persistent and intermittent AR presentations, regardless of symptom severity or disease duration. Studies focusing on other forms of rhinitis, additional nasal conditions, or participants with significant comorbidities will be excluded. No restrictions will be applied regarding participants demographics.

**Intervention** This review focuses on interventions using TCPMs specifically indicated for AR treatment, as listed in the ChP 2020. This encompasses a range of formulations, including tablets formulations like tongqiao biyan, xinqin, and xinyi biyan, granules formulations for tongqiao biyan and xinqin, tongqiao biyan capsules and xinyi biyan pills. Studies evaluating TCPMs in combination with western medical interventions are also eligible for inclusion, provided the analysis allows for the independent effects of the TCPMs to be clearly distinguished.

**Comparator** The review will consider studies employing comparators such as placebo, no active treatment, or western medical interventions for AR. These western medicine comparators may include, for instance, corticosteroids, antihistamines, or leukotriene receptor antagonists. However, studies that solely compare different Traditional Chinese medicine modalities without these other comparator groups will be excluded.

**Study designs to be included** Randomized controlled trials.

**Eligibility criteria** This review will exclude cross-over and before-after studies due to their limitations in determining causality. Duplicate publications will be identified and removed to ensure only unique data are included. Conference abstracts will also be excluded due to insufficient methodological detail.

**Information sources** This comprehensive literature search will encompass multiple electronic databases to identify eligible studies. These databases include Embase, Web of science, Pubmed, and Cochrane library, as well as Chinese databases such as Chinese Biomedical Literature Database (CBM), Chinese databases such as China National Knowledge Infrastructure (CNKI), VIP Information Chinese Journal Service Platform (VIP), Wanfang Data. In addition to these primary sources, the reference lists of included studies and pertinent systematic reviews will be screened for additional relevant publications.

**Main outcome(s)** ① Total Nasal Symptom Scores (TNSS). ② Total Ocular Symptom Scores (TOSS) or Total Eye Symptom Score (TESS). For inclusion, studies must report the TNSS or TOSS/TESS values, or the individual nasal symptom scores at one or more time points during or after the treatment period.

**Additional outcome(s)** ① Rhinitis Quality of Life Questionnaire (RQLQ) scores. ② Recurrence rates of symptoms associated with AR. ③ Nasal function, which include mucociliary clearance rate (MCR), nasal airway resistance (NAR), and mucociliary transport time (MTT). ④ Levels of biomarkers linked to AR, such as: TNF-α, IL-4, IL-5, IL-10, IL-13, and IgE. ⑤ Safety outcomes, the occurrence of specific adverse events, and any serious adverse events, which will be defined

according to the International Conference on Harmonisation (ICH) guidelines.

**Data management** To maintain a consistent and reliable database of research references, EndNote 21 will be used to manage study records. Any duplicate entries will be identified and removed.

**Quality assessment / Risk of bias analysis** To evaluate the risk of bias in the included RCTs, the Cochrane Risk of Bias tool (RoB 2.0) will be used. Two independent reviewers will assess each study for potential bias across five domains: randomization process, adherence to interventions, missing data, outcome measurement, and selective reporting. Each domain will be categorized as low risk, some concerns, or high risk. This assessment will be conducted at the outcome level to evaluate the impact of assignment. A third reviewer will be consulted to resolve any disagreements between reviewers regarding the risk of bias assessments. These assessments will be incorporated into the data synthesis and interpretation, and sensitivity analyses will be performed to explore the potential influence of studies with a high risk of bias on the overall conclusions.

**Strategy of data synthesis** To combine the results of the included studies, meta-analyses will be conducted using RevMan 5.4, if appropriate, based on the clinical similarity of the studies. For continuous outcomes, like TNSS, the analysis will involve calculating mean differences or standardized mean differences, along with 95% confidence intervals, using a random-effects model to account for variability across studies. For binary outcomes like adverse events, we will compute risk ratios accompanied by 95% confidence intervals, applying a random-effects model as well.

**Subgroup analysis** Subgroup analysis will explore the impact of factors like TCPMs dosage form, treament period, allergic rhinitis severity, or comparator type.

**Sensitivity analysis** Sensitivity analyses will be performed to determine how the results might change if studies with a high risk of bias are excluded.

**Language restriction** None.

**Country(ies) involved** China.

**Other relevant information** None

**Keywords** Chinese patent medicines, allergic rhinitis, 2020 Chinese Pharmacopoeia, protocol, systematic review, meta analysis.

**Contributions of each author**

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