International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

Intranasal natural products for influenza treatment: a systematic review and meta-analysis of preclinical studies

INPLASY2025120006

doi: 10.37766/inplasy2025.12.0006

Received: 2 December 2025

Published: 2 December 2025

Zhang, KQ; Lu, Y; Yang, JW; Shi, CQ; Zhao, N; He, XJ; Lv, C; Li, L.

Corresponding author:
Kaiqi Zhang

kayceezhang2021@163.com

Author Affiliation:
Institute Of Basic Research In Clinical Medicine, China Academy Of Chinese Medical Sciences.

ADMINISTRATIVE INFORMATION

Support - The work was supported by the National Key Research and Development Program of China (2023YFC3503400).

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY2025120006

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 2 December 2025 and was last updated on 2 December 2025.

INTRODUCTION

Review question / Objective Do natural products reduce relevant indicators in animal models of influenza? PICO principle: (1) Participants: Animal models infected with influenza virus; (2) Intervention: Influenza intervention using natural products via intranasal administration; (3) Comparison: The control group was an influenza virus-infected model group without treatment; (4) Outcomes: Primary outcomes included survival rate; secondary outcomes included viral titer, lung index, inflammatory cytokines, and body weight. Studies that included at least one of the above five outcomes were eligible for inclusion.

Condition being studied Influenza virus infections are infectious viral diseases characterized by high morbidity and mortality; these infectious diseases can trigger global pandemics. Clinical manifestations vary in severity: mild cases present only as common colds, with short disease duration, mild symptoms, and favorable prognosis, whereas severe cases may progress to influenza viral pneumonia or even be life-threatening.

METHODS

Search strategy We conducted searches of seven electronic databases—PubMed, Embase, Web of Science, China National Knowledge Internet (CNKI), VIP Information Chinese Periodical Service Platform (VIP), China Biology Medicine Disc (CBM), and Wanfang Data Knowledge Service Platform (Wanfang)—to identify relevant animal studies from database inception until December 2025. We used medical subject headings (MeSH) and free-text terms in our search, which were tailored for each database without language or publication year restrictions. The MeSH terms were as follows: ("influenza, human" OR "influenza A virus" OR "influenza B virus" OR "orthomyxoviridae") AND ("biological products" OR "phytochemicals" OR

"drugs, Chinese herbal" OR "herbal medicine" OR "phytotherapy" OR "plant extracts" OR "medicine, traditional" OR "medicine, east Asian traditional" OR "medicine, Korean traditional" OR "medicine, Tibetan traditional" OR "medicine, Mongolian traditional" OR "medicine, African traditional" OR "medicine, Chinese traditional" OR "medicine, Iranian traditional" OR "oils, volatile" OR "perfume") AND ("administration, intranasal" OR "nasal absorption" OR "nebulizers and vaporizers" OR "administration, inhalation" OR "Nasal sprays" OR "aromatherapy") AND ("animals" OR "animal experimentation").

Participant or population Participants: Animal models infected with influenza virus.

Intervention Intervention: Influenza intervention using natural products via intranasal administration.

Comparator Comparison: The control group was an influenza virus-infected model group without treatment.

Study designs to be included All animal studies focusing on natural products for influenza treatment via intranasalrespiratory tract administration will be included.

Eligibility criteria The inclusion criteria were based on the PICO principle: (1) Participants: Animal models infected with influenza virus; (2) Intervention: Influenza intervention using natural products via intranasal administration (e.g., nebulized inhalation, intranasal instillation, aerosol inhalation, etc.); (3) Comparison: The control group was an influenza virus-infected model group without treatment; (4) Outcomes: Primary outcomes included survival rate; secondary outcomes included viral titer, lung index, inflammatory cytokines, and body weight. Studies that included at least one of the above five outcomes were eligible for inclusion.
The exclusion criteria were as follows: (1) duplicated published literature; (2) reviews and editorials; (3) in vitro studies, clinical trials, or computer-based studies; (4) studies focusing on influenza prevention; (5) studies using nonintranasal administration routes; and (6) studies involving nonviral infections (e.g., bacterial or fungal infections).

Information sources PubMed, Embase, Web of Science, China National Knowledge Internet (CNKI), VIP Information Chinese Periodical Service Platform (VIP), China Biology Medicine Disc (CBM), and Wanfang Data Knowledge Service Platform (Wanfang).

Main outcome(s) Outcomes: Primary outcomes included survival rate; secondary outcomes included viral titer, lung index, inflammatory cytokines, and body weight.

Quality assessment / Risk of bias analysis The quality of the included studies was independently evaluated by two investigators using the SYRCLE risk-of-bias assessment tool for animal experiments. The evaluation criteria were as follows: (1) random sequence generation; (2) baseline characteristics; (3) allocation concealment; (4) random animal housing; (5) blinding of researchers; (6) random outcome assessment; (7) blinding of outcome assessment; (8) incomplete outcome data; (9) selective outcome reporting; and (10) other types of bias. "Yes" indicated low risk, "no" indicated high risk, and "unclear" indicated insufficient information to correctly assess the risk of bias (16). Any disagreements that arose during this phase of the project were resolved through the corresponding author (LL).

Strategy of data synthesis Data from the included studies were statistically analyzed using R Studio software. Heterogeneity among studies was assessed via the I^2 test. If the heterogeneity test results were $P \geq 0.1$ and $I^2 < 50\%$, indicating low heterogeneity between studies, a fixed-effects model was used for pooled effect size analysis; if $P < 0.1$ and $I^2 \geq 50\%$, indicating high heterogeneity between studies, a random-effects model was adopted for pooling. The effect sizes of the outcome measures were reported as follows: dichotomous outcomes were quantified using RR with 95% CI, and continuous outcomes were described using SMD with 95% CI. Statistical significance was determined by $P < 0.05$, and for dichotomous outcomes, the 95% CI did not include 1. The statistical heterogeneity of effect sizes was further quantified and evaluated using the I^2 value.

Subgroup analysis No subgroup analysis.

Sensitivity analysis We conducted a sensitivity analysis for the primary outcome measure (survival rate) in our meta-analysis by systematically excluding each study. This allowed us to assess the impact of the excluded study on the overall results and identify any influential studies.

Country(ies) involved China.

Keywords influenza, natural products, intranasal, meta-analysis, systematic review.

Contributions of each author

Author 1 - Kaiqi Zhang.
Email: kayceezhang2021@163.com
Author 2 - Yao Lu.
Author 3 - Jingwen Yang.
Author 4 - Changqi Shi.
Author 5 - Ning Zhao.
Author 6 - Xiaojuan He.
Author 7 - Cheng Lv.
Author 8 - Li Li.