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Protective effects and mechanism of traditional Chinese medicine polysaccharides in bleomycin-induced pulmonary fibrosis in animal models: a preclinical systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION**Support** - No support.**Review Stage at time of this submission** - Completed but not published.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202690008

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 2 September 2026 and was last updated on 2 September 2026.

INTRODUCTION

Review question / Objective Pulmonary fibrosis (PF) is a progressive and fatal interstitial lung disease with limited therapeutic options. Traditional Chinese medicine (TCM) polysaccharides have demonstrated promising anti-fibrotic effects in animal models of bleomycin-induced PF, but the evidence has not been systematically evaluated. This review will provide the first comprehensive quantitative synthesis of TCM polysaccharides in preclinical PF models and explore potential mechanisms, thereby supporting translational research and clinical development.

Condition being studied Bleomycin-induced pulmonary fibrosis in animal models (any species).

METHODS

Search strategy A comprehensive search will be conducted in PubMed, Web of Science, CNKI

(China National Knowledge Infrastructure), and WanFang Data from inception to August 2026, using combinations of MeSH terms and free-text keywords covering the following blocks: (1) pulmonary fibrosis OR idiopathic pulmonary fibrosis OR bleomycin OR BLM; (2) polysaccharide OR glucan OR glycan OR beta-glucan OR mannan OR fructan OR saccharide; (3) Chinese medicine OR Chinese herbal OR TCM OR names of specific medicinal herbs (e.g., Astragalus, Angelica, Poria, Ophiopogon, Lycium, Dendrobium, Panax, Ganoderma, Codonopsis, Lilium, Bletilla, Cordyceps, Ophiocordyceps, Hedysarum, Brassica rapa, Polyporus, Achyranthes) and their Chinese equivalents. The full search strategies for each database will be provided in the supplementary material.

Participant or population Animals (mice, rats, or other species) with bleomycin-induced pulmonary fibrosis, regardless of strain, sex, age, or weight.

Intervention Polysaccharides extracted and purified from traditional Chinese medicine herbs, administered via any route (oral gavage, intraperitoneal injection, etc.), at any dose and duration. When multiple dose groups are reported, the highest dose group will be selected for analysis.

Comparator Model control animals receiving the same volume of vehicle (normal saline, distilled water, or CMC-Na) or no treatment. Studies without a model control group will be excluded.

Study designs to be included Controlled animal studies (randomized or non-randomized) evaluating TCM polysaccharides in bleomycin-induced PF. Reviews, conference abstracts, in vitro studies, human studies, and clinical trials will be excluded.

Eligibility criteria Inclusion: (1) bleomycin-induced PF model; (2) intervention is a polysaccharide from a TCM herb (crude polysaccharide or purified polysaccharide fraction); (3) presence of a model control group; (4) reporting at least one target outcome (HYP, lung coefficient, Ashcroft score, or Masson collagen area percentage). Exclusion: (1) non-bleomycin models (e.g., silica, paraquat, radiation, LPS); (2) polysaccharides combined with other active drugs or cells (combined interventions); (3) studies reporting only inflammatory cytokines or oxidative indicators without fibrosis outcomes; (4) duplicate publications of the same experiment (merged as one study); (5) conference abstracts, reviews, or studies without full text.

Information sources Electronic databases: PubMed, Web of Science, CNKI, and WanFang Data (search date: August 2026). No language restrictions will be applied. Reference lists of included studies will be screened for additional eligible studies (backward citation chasing). Grey literature will not be systematically searched, and this limitation will be reported.

Main outcome(s) Primary outcome: hydroxyproline (HYP) content in lung tissue. Secondary outcomes: lung coefficient (lung weight/body weight), Ashcroft score (0–8 scale), Masson collagen area percentage. Time points: if multiple time points are reported, the final (latest) time point will be used; when data are presented only in graphs, WebPlotDigitizer will be used to extract mean and standard deviation values.

Quality assessment / Risk of bias analysis The methodological quality of included studies will be

assessed independently by two reviewers using the SYRCLE's Risk of Bias (RoB) tool (10 items), rated as "yes" (low risk), "no" (high risk), or "unclear". Disagreements will be resolved by discussion or consultation with a third reviewer.

Strategy of data synthesis All outcomes are continuous variables; the standardized mean difference (SMD) with 95% confidence intervals (CIs) will be used as the effect measure. Heterogeneity will be assessed using the I^2 statistic: $I^2 \leq 50\%$ indicates acceptable heterogeneity (fixed-effect model); $I^2 > 50\%$ indicates substantial heterogeneity (random-effects model). Analyses will be performed using R software (version 4.x) with the metafor package.

Subgroup analysis Pre-specified subgroup analyses will be performed to explore sources of heterogeneity based on: animal species (mice vs. rats), route of administration (oral vs. injection), polysaccharide type/herb, intervention timing (preventive vs. therapeutic), and positive drug control.

Sensitivity analysis Sensitivity analysis will be conducted by omitting one study at a time (leave-one-out) to assess the robustness of the pooled results.

Country(ies) involved China.

Keywords No language restrictions will be applied. Keywords: pulmonary fibrosis, bleomycin, polysaccharide, traditional Chinese medicine, meta-analysis, animal model.

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