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Protective effects and mechanism of Curcumin in animal models of pulmonary fibrosis: A preclinical systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - NO.2019YFC1712000.

Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 27 June 2023 and was last updated on 04 July 2023.

INTRODUCTION

Review question / Objective Pulmonary fibrosis (PF) as a chronic interstitial lung disease is characterized by damage to the lung epithelium, accumulation of fibroblasts, and deposition of collagen-rich extracellular matrix, which may lead to decreased gas exchange and lung compliance, with exercise-induced dyspnea and chronic dry cough being the prominent symptoms. In contrast, idiopathic pulmonary fibrosis (IPF), a disease characterized by progressive dyspnea with no specific cause, has an increasing incidence, prevalence, and mortality rate year by year, with an extremely poor prognosis and a median survival of 3-5 years, affecting approximately 3 million people worldwide and imposing a severe economic burden on patients.

Condition being studied Curcumin is an acidic polyphenol, a diketone, which is widely found in the rhizomes of many plants, such as Curcuma longa, Curcuma longa, Tulip tree and Acorus calamus. Many studies have demonstrated that CUR can attenuate the pathological progression of various fibrosis models, such as in oral submucous fibrosis, Liver fibrosis, and Renal fibrosis, which has led to widespread interest in its antifibrotic effects.The antifibrotic mechanism of CUR is related to the reduction of collagen accumulation and, in addition, CUR reduces the expression of matrix metalloprotein (MMP)-2 and MMP-9, which are structurally remodeled in pulmonary fibrosis.

METHODS

Search strategy To identify relevant animal studies without language restrictions, publications from January 1, 2000 to April 19, 2023 were systematically searched from four electronic databases, Pubmed, Embase, Web of Science, and the Cochrane Library.

Participant or population Animal studies.

Intervention Treatment group received any dose, time, frequency and any mode of administration of curcumin as a single treatment.

Comparator This includes moulding only, or receiving the same amount of non-functional fluid or no treatment.

Study designs to be included Only animal studies that assessed the protective effects of Curcumin in animal models of PF were included regardless of publication statuso language.

Eligibility criteria We included controlled studies assessing the administration of Curcumin for in animal models of PF stablished by different methods, regardless of animal species, age, weight and gender.

Information sources Electronic searches were conducted in four databases with no language restrictions from January 1, 2000 to 19 April 2023: Pubmed, Embase, Web of Science and the Cochrane Library.

Main outcome(s) The primary outcome was hydroxyproline content.

Additional outcome(s) The additional outcome measures MPO activity, MDA, NO, GSH, PaO2, the concentration of TNF-α, and TGF-β.

Quality assessment / Risk of bias analysis The Systematic Review Center for Laboratory Animal Experiments (SYRCLE) risk of bias was used.

Strategy of data synthesis Revman 5.3 and Stata 16. were used to integrate data from all included studies, and given that all outcome indicators were continuous variables, standardized mean differences (SMDs) with 95% confidence intervals (CIs) were used to express effect sizes. Heterogeneity between studies and subgroups was assessed by I2, and when the heterogeneity of included studies was small (I2 ≤ 50%), a fixed-effects model was used for analysis; when I2 > 50%, a random-effects model was used for analysis. If the heterogeneity of the included studies was large, sensitivity analyses were performed to assess the stability of the overall results, and if sufficient studies were available, subgroup analyses were used to assess sources of heterogeneity and publication bias by funnel plot, Egger test, and Begg's test.

Subgroup analysis Six subgroups were pre-specified to assess the effect of variables or study characteristics on the estimated effect sizes: (1) animal species, (2) animal sex, (3) route of administration, (4) intervention time point, (5) treatment duration and (6) animal modeling methods.

Sensitivity analysis If the heterogeneity of the included studies was high, sensitivity analyses were performed to assess the stability of the overall results.

Country(ies) involved China.

Keywords Curcumin; PF; IPF ; Animal Models.

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