

**Protective effects and mechanism of Curcumin in animal models of acute lung injury: A preclinical systematic review and meta-analysis**

INPLASY202360047

doi: 10.37766/inplasy2023.6.0047

Received: 15 June 2023

Published: 16 June 2023

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Hong, Z<sup>1</sup>; Fang, HY<sup>2</sup>; Liu, Y<sup>3</sup>; Zhang, HC<sup>4</sup>; Dong, WJ<sup>5</sup>; Liu, MF<sup>6</sup>.**ADMINISTRATIVE INFORMATION****Support** - NO.2019YFC1712000.**Review Stage at time of this submission** - Data analysis.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202360047**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 16 June 2023 and was last updated on 16 June 2023.**INTRODUCTION**

**Review question / Objective** Acute Lung Injury (ALI)/ Acute Respiratory Distress Disorder (ARDS) As a devastating respiratory disease characterised by acute respiratory failure, refractory hypoxaemia and non-cardiogenic pulmonary oedema, ARDS is considered to be a severe stage of ALI and both share similar pathophysiological changes. Results of a 50-country/regional survey showed that ARDS accounts for 10.4% of ICU admissions, is difficult to identify early and poorly diagnosed, and has a mortality rate of 46.1% in severe cases.

**Condition being studied** Curcumin is considered to be the main active component of turmeric and its anti-inflammatory and antifibrotic effects in vivo have become a focus of innovation and a hot topic of medical research. Many studies have confirmed that CUR inhibits inflammatory cell activation and promotes a reduction in the production of inflammatory cytokines, including IL-8, IL-6 and TNF- $\alpha$ . In addition, CUR with antifibrotic properties

reduces collagen accumulation in the lung. Moreover, CUR scavenges free radicals and improves redox imbalance.

**METHODS**

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

**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.

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**Study designs to be included** Only animal studies that assessed the protective effects of Curcumin in animal models of ALI/ARDS were included regardless of publication status or language.

**Eligibility criteria** We included controlled studies assessing the administration of Curcumin for in animal models of ALI/ARDS established 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 the build deadline to 19 April 2023: Pubmed, Embase, Web of Science and the Cochrane Library.

**Main outcome(s)** The primary outcome measures were acute lung injury specific index:wet/dry weight of animal lung and balf protein.

**Additional outcome(s)** The additional outcome measures EBD, MPO activity, MDA, the concentration of TNF- $\alpha$ , IL-6, IL-1 $\beta$ , IL-10, NO and HYP.

**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 I<sup>2</sup>, and when the heterogeneity of included studies was small (I<sup>2</sup>  $\leq$  50%), a fixed-effects model was used for analysis; when I<sup>2</sup> > 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 models of direct or indirect lung injury.

**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; ALI; ARDS; Animal Models.

**Contributions of each author**

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