

INPLASY

Protective role of curcumin in the dynamic progression of asthma: 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 30 September 2023 and was last updated on 30 September 2023.

INTRODUCTION

Review question / Objective Bronchial asthma is a heterogeneous disease characterised by airway inflammation and airway hyperresponsiveness (AHR), the clinical manifestations of which can be variable airflow obstruction and respiratory symptoms such as wheezing, coughing, chest tightness, and dyspnoea. Asthma, as one of the most common respiratory diseases, has a cumulative prevalence of between 4.2% and 9.9% in some countries. Asthma involves a number of complex pathophysiological mechanisms, such as allergen-induced immune response and lung injury stimulating airway inflammation, airway remodelling, AHR and oxidative imbalance. Whereas in animal models relevant asthma features can be simulated and new therapeutic targets can be identified and evaluated, such as acute provoked asthma model to reproduce airway inflammation and AHR, chronic provoked asthma model to reproduce airway remodelling and

persistent AHR, etc., and acute provoked model to simulate acute exacerbation of inflammation.

Condition being studied Curcumin (CUR), as a natural polyphenolic compound, is considered to be the main active ingredient of turmeric. CUR possesses a variety of properties such as anti-inflammatory, immunomodulatory, antioxidant, antifibrotic and antitumour. CUR has been widely used in the treatment of a variety of heterogeneous disorders, such as allergic rhinitis, rheumatoid arthritis, ulcerative colitis, and systemic lupus erythematosus, etc., and exerts its therapeutic effects by mediating and regulating a variety of cellular signal transduction pathways, cellular and transcription factors.

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 July 10, 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.

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

Eligibility criteria We included controlled studies assessing the administration of Curcumin for in animal models of Asthma 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 July 10, 2023: PubMed, Embase, Web of Science and the Cochrane Library.

Main outcome(s) Immunoglobulin(Ig)E level as the Primary Outcome Indicator.

Additional outcome(s) Secondary outcome indicators included the following: inflammation-related indicators (including nitric oxide (NO), eosinophil peroxidase (EPO) activity, myeloperoxidase (MPO) activity, histamine, interleukin (IL)-4, IL-5, interferon (IFN)- γ , and tumor necrosis factor (TNF)- α concentrations), and airway remodelling-related indices (including hydroxyproline (HYP) content, IL-13, matrix metalloprotein (MMP)-9 activity, the bronchoprotective function, and the bronchoprotective function). activity, the bronchial wall thickness (Wat), the thickness of the smooth muscle layer (Wam)), redox-related indices (including reactive oxygen species (ROS), malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT)), AHR-related indices (enhanced pause (Penh) values during 10mg/ml acetylcholine (Ach), 12.5 mg/ml Ach, 25 mg/ml Ach, 50 mg/ml Ach excitation), safety-related indicators (including alanine transaminase (ALT), aspartate transaminase (AST), creatinine (CRE)).

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

Strategy of data synthesis Stata 16 and R 4.3.1 were used to integrate data from all included studies, and given that all outcome indicators were continuous variables, effect sizes were expressed through standardized mean deviations (SMDs) with 95% confidence intervals (CIs). Heterogeneity between studies and subgroups was assessed by I² and Q-tests; when heterogeneity of included studies was small (I² \leq 50%), it was analyzed using a fixed-effects model; when I² > 50%, it was analyzed using a random-effects model. If the heterogeneity of the included studies was large, sensitivity analyses were performed to assess the stability of the overall results; for outcome metrics that included more than 10 studies, meta-regression and subgroup analyses were used to assess the sources of heterogeneity, and publication bias was assessed by funnel plots, Egger's test, and Begg's test. Graphpad Prism 9.5 and Origin 2021 were used to report the results, respectively. Stratified meta-analysis and analysis of dose-time-effect relationship. $p \leq 0.05$ was considered statistically significant.

Subgroup analysis Seven subgroups were prespecified to assess their influence on the effect size: (1) animal species, (2) CUR single administration dose, (3) CUR route of administration, (4) acute or chronic provocation model of asthma, (5) whether an acute exacerbation occurred, (6) intervention timing, and (7) duration of treatment. In addition, subgroup analyses can be used to track sources of heterogeneity.

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; Asthma; Animal Models.

Contributions of each author

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