INPLASY PROTOCOL

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Review Stage at time of this submission: **The review has not yet started.**

Conflicts of interest: **No.**

Effects of Cinnamaldehyde on Anti-Respiratory Syncytial Virus: a protocol of systematic review and meta-analysis

Feng, L[1]; Li, J[2]; Yu, HB[3]; Xue, Q[4]; Dai, LJ[5].

Review question / Objective: **Is cinnamaldehyde effective on anti-Respiratory Syncytial Virus (ARSV)?**
Condition being studied: **Cinnamaldehyde; anti-Respiratory Syncytial Virus.**
Information sources: **This study will search MEDLINE, EMBASE, Cochrane Library, Cumulative Index to Nursing and Allied Health Literature, Technology Periodical Database, China Biology Medicine, and China National Knowledge Infrastructure from their outset to the March 31, 2020 without restrictions of language and publication time. We will consider all potential case-controlled studies (CCSs) or randomized controlled studies (RCSs) that examined the effects of cinnamaldehyde on ARSV for inclusion. A detailed search strategy for MEDLINE is summarized. Identical search strategies with specifics will be adapted and applied to the other electronic databases. We will also search other resources, such as relevant conference proceedings, and reference lists of included studies.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 13 April 2020 and was last updated on 13 April 2020 (registration number INPLASY202040074).

INTRODUCTION

Review question / Objective: **Is cinnamaldehyde effective on anti-Respiratory Syncytial Virus (ARSV)?**

Condition being studied: **Cinnamaldehyde; anti-Respiratory Syncytial Virus.**

METHODS

Participant or population: **This study will include respiratory syncytial virus infects host HeLa cells as its research targets.**

Intervention: **In the experimental group, all studies utilized cinnamaldehyde alone for the treatment of ARSV.**

Comparator: In the control group, studies used any comparators will be included, such as no treatment, any other anti-virus treatments. However, we will not include studies using cinnamaldehyde.

Study designs to be included: All case-controlled studies (CCSs) or randomized controlled studies (RCSs) exploring the effects of cinnamaldehyde on ARSV will be included.

Eligibility criteria: This study will include all potential CCSs or RCSs exploring the effects of cinnamaldehyde vs. other comparators on ARSV.

Information sources: This study will search MEDLINE, EMBASE, Cochrane Library, Cumulative Index to Nursing and Allied Health Literature, Technology Periodical Database, China Biology Medicine, and China National Knowledge Infrastructure from their outset to the March 31, 2020 without restrictions of language and publication time. We will consider all potential case-controlled studies (CCSs) or randomized controlled studies (RCSs) that examined the effects of cinnamaldehyde on ARSV for inclusion. A detailed search strategy for MEDLINE is summarized. Identical search strategies with specifics will be adapted and applied to the other electronic databases. We will also search other resources, such as relevant conference proceedings, and reference lists of included studies.

Main outcome(s): Primary outcome is apoptotic host HeLa cells, as detected by flow cytometry.

Additional outcome(s): Secondary outcomes are apoptosis-related proteins expression, as measured by immunofluorescence or western blot test. These proteins include Caspase-3, Caspase-9, p-AKT, Bcl-2, and Bax.

Data management: Two researchers will independently extract data using a previous designed data extraction template. It consists of study characteristics (such as title, first author, journal, et al), information of targeted Host cell Hela, study design (such as types of study, sample size, et al), intervention and control details (such as types of treatments, dosage, et al), outcomes, results, findings, and other related information. In case of unclear or missing data, we will contact primary authors to obtain it. Any uncertainties will be solved by discussion with a third researcher involved.

Quality assessment / Risk of bias analysis: Two researchers will independently assess study quality for each included studies. The study quality of CCSs will be evaluated by Newcastle-Ottawa Scale, and study quality of RCSs will be appraised by Cochrane risk of bias tool. Any unconsensuses will be resolved by discussion with the help of a third researchers invited.

Strategy of data synthesis: Statistical analyses will be undertaken by RevMan 5.3 software. We will use risk ratio and 95% confidence intervals (CIs) to calculate dichotomous data, and will utilize mean difference or standardized mean difference and 95% CIs to present continuous data. We will check heterogeneity using I^2 test. $I^2 \leq 50\%$ means homogeneity, and use a fixed-effects model will be employed. If possible, we will also conduct a meta-analysis. $I^2 > 50\%$ indicates remarkable heterogeneity, and we will utilize a random-effects model. In addition, we will perform a subgroup analysis to examine the possible sources of obvious heterogeneity.

Subgroup analysis: We will perform a subgroup analysis based on the types of studies, different intervention and controls, and outcomes.

Sensibility analysis: We will carry out a sensitivity analysis to test the stability for study findings by removing low methodological quality studies.

Country(ies) involved: China.

Keywords: Cinnamaldehyde; anti-Respiratory Syncytial Virus; effect.