

**The Potential of Echinacea in Reducing Recurrent Respiratory Tract Infections, their Complications and the Associated Need for Antibiotics: A Meta-Analysis**

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**Review question / Objective** Examine whether Echinacea supplementation could help in reducing the need for antibiotic prescriptions through the prevention and/or acute treatment of recurring respiratory tract infections (RTI) and their complications?

**Rationale** Viral Respiratory Tract Infections (vRTI) are the main reason for prescribing antibiotics (AB) in humans. ABs are given to avoid worsening of initial viral into potentially fatal, secondary bacterial superinfections associated with sinusitis, otitis media or the lethal pneumonia.

There are severe implications with antibiotic use; for instance the various gastrointestinal side effects or the risk of anaphylaxis. More significantly, the excessive use of antibiotics gives rise to the threat of antibiotic resistance. The reason for antibiotic resistance is the occurrence of a random genetic mutation that allows for the

survival of the specific bacteria against the antibiotic administered. The misuse of antibiotics (e.g. for the treatment of viral RTIs) acts as a catalyst to the emergence of resistance. An effective way to overcome or slow down the development of resistances would be to reduce RTIs, the foremost initiator for antibiotic use.

The medicinal plant Echinacea exhibits antiviral and immune-modulatory properties that allow for the prevention of viral RTI, with all their consequences, i.e. secondary complications. This meta-analysis will be about whether Echinacea may also be able to decrease the use of antibiotics.

**Condition being studied** Respiratory Tract Infection are mostly viral but can be preceded by bacterial superinfections, including tonsillitis, sinusitis or the feared pneumonia. Many physicians prescribe antibiotics to patients in order to prevent those exacerbations. Therefore, RTIs represent the foremost cause for antibiotic overuse in humans.

## METHODS

**Search strategy** Screen the available literature on MEDLINE, Google Scholar and EMBASE from inception to 06/2023 for terms Echinacea (all species), coneflower, Roter Sonnenhut without restriction for language. Systematic reviews, which assess primary data of Echinacea as a treatment intervention published between 1980 – 2023 will be included, regardless of the language. They must also be free to access in full online. In order to translate systematic reviews which are not accessible to the reviewer without linguistic aids (namely German) free online translation software will be used. This review will consider all controlled, randomized studies that involve human participants of any age, female and males taking Echinacea for the acute treatment or prevention of respiratory infections. Interventions of interest included those related to efficacy and/or effectiveness of Echinacea as a treatment by including specific clinical interventions and follow up assessment strategies. The primary outcome of interest is whether intake of Echinacea is associated with a reduced occurrence of recurring RTI, secondary complications<sup>1</sup>) (worsening during acute treatment or prevention) and whether this could overall lead to a reduced need for antibiotics. To this end, only studies including reasonable control (placebo, non-treatment (if effectively randomized) active control or history) will be regarded. Studies indicating occurrence of RTI (complications), bacterial superinfections and/or use of AB in Echinacea-treatment human subjects are selected. Data will be presented in tabulated form to allow for comparison of Echinacea species/dosis/preparation used, sample size, incidence of RTI (complications), AB applications and duration. A differentiation into acute treatment and prevention studies might be preferred.

**Participant or population** This review principally includes healthy participants or those with acute respiratory tract infections.

**Intervention** Echinacea.

**Comparator** Placebo, non-treatment (if randomized), active control, history (optional).

**Study designs to be included** Randomized controlled clinical studies involving humans.

**Eligibility criteria** Studies will be included into analysis, which report on occurrence of recurrent respiratory tract infections, their complications / bacterial superinfections, including eg. Tonsillitis,

Pharyngitis, Tracheitis, Lymphadenitis, Bronchitis, Pneumonia, Sinusitis, (bacterial) Conjunctivitis, Otitis Media, or information from respiratory adverse events.

**Information sources** Screen the available literature on MEDLINE, Google Scholar and EMBASE from inception to 04/2023 for terms Echinacea (all species), coneflower, Roter Sonnenhut without restriction for language.

**Main outcome(s)** Occurrence of recurrent respiratory tract infections; Occurrence of RTI complications; Use of Antibiotics and duration of use; Upon application of Echinacea.

**Quality assessment / Risk of bias analysis** Data will be extracted and analysed by at least two reviewers to resolve any disagreements. Risk of bias and quality for each included trial will be independently assessed by the same reviewers. CONSORT check list will be used to assess agreement between reviewers.

**Strategy of data synthesis** Odds ratios will be calculated expressing rates of patients with (recurrent) RTIs, complications and antibiotic use respectively. Furthermore number of (recurrent) RTIs, complications and antibiotic treatment cycles will be expressed with odds ratios between patients supplemented with Echinacea and the control group. Duration of antibiotic therapy will be analysed as well.

**Subgroup analysis** The main analysis will cast a wide net on all products containing Echinacea, no matter which extraction or application form to detect for generally applicable effects. Subgroup analysis will focus on interventions containing Echinacea alone, while excluding combination products with e.g. vitamins or minerals. Studies might be grouped into treatment versus prevention approaches. Further subgroups are to be formed in order to more accurately understand the mode-of-action of Echinacea.

**Sensitivity analysis** Sensitivity analysis will be carried out while in- or excluding particular studies in relation to the respective research question.

**Language restriction** English, German French, Italian.

**Country(ies) involved** United Kingdom, Canada, German, Switzerland.

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**Keywords** Echinacea, Respiratory Tract Infections, Complications, Antibiotic overuse, Prevention, Acute Treatment.

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