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**File: ■ Echinacea (*Echinacea* spp., Asteraceae)  
■ Respiratory Tract Infections  
■ Meta-analysis**

**HC 071566-534**

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**RE: Meta-analysis Concludes Echinacea Extracts Safely Reduce Risk of Respiratory Tract Infection Recurrence and Complications**

Schapowal A, Klein P, Johnston SL. Echinacea reduces the risk of recurrent respiratory tract infections and complications: a meta-analysis of randomized controlled trials. *Adv Ther.* March 2015;32(3):187-200.

Respiratory tract infections (RTIs), including colds and flu, may disrupt quality of life and are often recurrent or lead to complications. Complications include severe medical conditions like bronchitis or pneumonia, which are associated with high morbidity and mortality. Avoiding complications is the main motive for prescription of antibiotics during colds and flu infections, as currently no preventive therapy is available. Echinacea (*Echinacea* spp., Asteraceae) has traditionally been used by Native Americans,<sup>1</sup> and in contemporary times is used for the prevention and treatment of RTIs. Previous preclinical studies have shown echinacea to have anti-inflammatory, antiviral, and immunomodulatory bioactivity. This meta-analysis analyzed clinical studies of echinacea effects on RTI recurrence and complications from these infections.

A literature search was conducted in the MEDLINE, EMBASE, CAbplus, BIOSIS, CABA, AGRICOLA, TOXCENTER, SCISEARCH, NAHL, and NAPRALERT databases using "echinacea," "black Sampson," "coneflower," and "Roter Sonnenhut." Trials with a randomized, placebo-controlled study design using echinacea in healthy subjects over two to four months for the prevention of recurrent RTIs were screened. The Jadad score  $\geq 4$  was used to assure adequate study quality (lower scores indicate lower quality). Recurrent RTI was the primary outcome, as measured by number of RTIs or number of subjects with repeat RTIs. Data were pooled for the meta-analysis, and RTI recurrence and complications in those taking echinacea or placebo were compared with the "underlying populations." [Note: This term is not further defined; presumably, it refers to the total number treated in each group.] Complications included conjunctivitis, sinusitis, otitis (ear inflammation), tonsillitis, pharyngitis, bronchitis, and pneumonia. Antibiotic use also was assessed, and adverse side effects were noted.

When using the search term "echinacea," 101 clinical trials were found. Of these, 89 did not meet the inclusion criteria. From the remaining 12, six were further eliminated due to

low Jadad score ( $\leq 3$ ), "artificial inoculation" without recurrence follow-up, and secondary analysis of study subgroups. One study included material from both *E. angustifolia* and *E. purpurea* in a three-arm study; data from both treatment groups were pooled and compared to placebo. Four trials used ethanol/glycerol extracts of *E. angustifolia* and *E. purpurea*, and two trials incorporated *E. purpurea* pressed juice. It is mentioned that these different types of preparations likely contain distinctive compounds (lipophilic vs. hydrophilic, respectively).

Also, in the study with the most subjects ( $n=757$ ), not only were symptoms reported by subjects used for constituting an RTI, but subjects were also virally tested. Although only two of the studies analyzed reported significantly decreased relative risk ratios (RRs) (averaged=0.498; 95% confidence intervals [CI] 0.386-0.642;  $P<0.0001$ ), the meta-analysis still revealed an RR of 0.649 (95% CI 0.545-0.774;  $P<0.0001$ ). RRs of 0.663 and 0.734 were seen in the two largest studies that both utilized alcohol extracts of echinacea ( $P$  value not reported). Heterogeneity was indicated and considered quantitative rather than qualitative due to similar positive results across studies.

In the four studies with subjects having recurring RTIs, a significantly lower RR for echinacea was observed (0.769; 95% CI 0.598-0.990;  $P=0.041$ ). When analyzing lipophilic extracts and juice preparations in the prevention of recurrent RTIs, the RR for the alcoholic extracts was significantly reduced (0.542; 95% CI 0.432-0.679;  $P<0.0001$ ); however, the RR for echinacea juices was not significantly different from the comparison population (0.858; 95% CI 0.649-1.135;  $P=0.283$ ).

Of the three studies that investigated the presence of complications, there was a significantly decreased RR in those taking echinacea (0.503; 95% CI 0.384-0.658;  $P<0.0001$ ). The 50% overall decreases in complications included a 64.9% reduction in pneumonia and similar outcomes for otitis and tonsillitis ( $P<0.0001$ ,  $P<0.0001$ , and  $P=0.021$ , respectively).

In three studies, antibiotic use declined in those using echinacea as compared with control or standard treatment, although significance is not mentioned. Among 1,440 subjects taking echinacea and 1,326 subjects taking placebo, the amount of adverse side effects was comparable (491 vs. 474, respectively). Gastrointestinal complaints were most common, and considered "mild." Two serious cases of troubled breathing were seen with *E. purpurea* pressed juice treatment and glandular fever was observed in a subject taking placebo. Despite this, laboratory parameters were not different between groups over four months. Subjects mostly rated the tolerance of echinacea as "good" or "very good."

This meta-analysis suggests that echinacea consumption significantly prevents the recurrence of RTIs in generally healthy subjects and also in susceptible individuals exposed to stress, smokers, and those with poor sleep. Additionally, echinacea was shown to prevent specific RTI complications and may have reduced antibiotic usage. Taken together, these results suggest obvious benefits from the usage of echinacea for prevention of RTI recurrence and complications. In view of the great medical and socio-economic impact of complications (loss of productivity, morbidity, and finally, mortality), these findings are highly significant.

One potential weakness of this study is lack of details regarding study preparations, products, and plant parts used. Two clinical trials used echinacea products with

additional supplements. Additional benefits from these supplements remain uncertain. The largest study employed a pure *E. purpurea* extract (95% herb and 5% roots, Echinaforce®; A. Vogel Bioforce AG; Roggwil, Switzerland) and gave a result that was very similar to the overall observed effects. Thus, it is very likely that the identified effects are due to echinacea. Of particular interest are the studies using different types of echinacea extracts (lipophilic vs. hydrophilic) and the difference observed in RR. Ideally, future studies with this genus will focus on specific bioactivity, such as RTI recurrence prevention and the particular plant parts and preparations with different potential active compounds.

—Amy C. Keller, PhD

#### Reference

<sup>1</sup>Blumenthal M, Goldberg A, Brinckmann J, eds. *Herbal Medicine: Expanded Commission E Monographs*. Austin, TX: American Botanical Council; Newton, MA: Integrative Medicine Communications; 2000.

The American Botanical Council has chosen not to include the original article.

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