Echinacea for preventing and treating the common cold (Review)

Melchart D, Linde K, Fischer P, Kaesmayr J

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ABSTRACT

Background
Extracts of the plant Echinacea (family Compositae) are widely used in some European countries and the USA for upper respiratory tract infections.

Objectives
The objective of this review was to assess the effects of preparations containing extracts of Echinacea in the prevention and treatment of the common cold.

Search strategy
We searched the Cochrane Acute Respiratory Infections Group and Complementary Medicine Field's trials registers, MEDLINE, EMBASE, Phytodok and reference lists of articles. We also contacted researchers and manufacturers. Date of last search: Spring 1998.

Selection criteria
Randomised and quasi-randomised trials comparing preparations containing an extract of Echinacea compared with a placebo, no treatment, or another treatment for common colds.

Data collection and analysis
At least two independent reviewers assessed trial quality and extracted data.

Main results
Sixteen trials (eight prevention trials, and eight trials on treatment of upper respiratory tract infections) with a total of 3396 participants were included. Variation in preparations investigated and methodological quality of trials precluded quantitative meta-analysis. Overall, the results suggested that some Echinacea preparations may be better than placebo.

Authors' conclusions
The majority of the available studies report positive results. However there is not enough evidence to recommend a specific Echinacea product, or Echinacea preparations for the treatment or prevention of common colds.

SYNOPSIS
Echinacea preparations can probably help prevent and treat common colds, although more research is needed.

Extracts of the plant Echinacea are widely used in several countries to prevent or treat the common cold. When taken by mouth, the risk of adverse effects is small. In Germany alone, there are more than 200 different Echinacea preparations on the market. The review found it difficult to compare Echinacea trial results, as the preparations varied greatly. Overall, the evidence from trials suggests that
some Echinacea preparations can probably help prevent and treat the common cold. However, there is not enough evidence to support a particular product or type of preparation.

**BACKGROUND**

Extracts of the plant Echinacea (family Compositae) are widely used by patients and practitioners in some European countries (for example the Netherlands and Germany) and in the USA for preventing and treating upper respiratory tract infections. On the German market there are at present more than 200 preparations obtainable which contain extracts of Echinacea alone or in combination with other plant extracts. In 1993 for the five leading preparations in Germany prescriptions of over 3 million daily doses with a cost of 50 million DM (about $35 million) were registered (Haustein 1994). Although the prescription of extracts of Echinacea by physicians has decreased in the last years (for example from 1992 to 1993 between 21 and 35% for the five market leading preparations (Haustein 1994)), this has probably at least in part been compensated for by an increase of over-the-counter use.

Extracts of Echinacea contain varying concentrations of flavonoids, essential oils, polysaccharides, derivates of caffeic acid, polycyctenes, alkylamides and alkaloids. The stimulation of non-specific immune defence capacities, such as phagocytosis of polymorphonuclear neutrophile granulocytes, has been postulated as the mechanism of action (Bauer 1990).

Despite its widespread use, there is considerable debate about the effectiveness of Echinacea, and doubts have been raised about safety in the (relatively rare) case of parenteral (intravenous or intramuscular) application (Schönhöfer 1989, Bauer 1996).

The assessment of effectiveness is complicated by the limited comparability of the available preparations for the following reasons:
1) Three different species are in medical use: Echinacea (E.) purpurea, E. pallida, and E. angustifolia.
2) Different parts of the plant are used (roots, herbs, whole plant).
3) Different methods of extraction are used.
4) In some preparations other plant extracts or homeopathic components are added.

**OBJECTIVES**

In 1994 our group published a systematic review of the available controlled clinical trials (also including non-randomized trials) investigating preparations containing extracts of Echinacea in a variety of conditions (Melchart 1995a). Our objective now was to perform a more detailed review focussing on the assessment of the available evidence from randomized clinical trials investigating the effectiveness of Echinacea extracts for the prevention and the treatment of the common cold.

**CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW**

**Types of studies**

Prospective clinical trials with random or quasi-random (such as alternation, date of birth etc.) allocation to treatment and control groups.

**Types of participants**

Studies were included if participants were:
- patients with unspecified viral upper respiratory tract infections (URTI; clinical diagnoses: common cold, influenza-like syndrome, viral URTI - it was not possible to apply a standard definition of common cold across all trials)
- volunteers without acute upper respiratory tract infections but treated for preventative purposes (prevention studies).

Studies on patients suffering from other upper respiratory tract infections with a defined etiology (e.g. influenza) or a more specific symptomatology (acute sinusitis, angina tonsillaris) were not included.

**Types of intervention**

Treatment group: Application of preparations containing extracts of Echinacea either as the only component (mono-preparations) or in combination with other plant extracts.

Control group: Other strategies (other therapy, no treatment, placebo)

**Types of outcome measures**

To be included in the overview trials must include clinical outcome measures related to occurrence (prevention studies), severity or duration (treatment studies) of infections. Trials focussing solely on physiological parameters (such as phagocytosis activity etc.) were excluded.

**SEARCH STRATEGY FOR IDENTIFICATION OF STUDIES**

See: search strategy

The following sources were searched:
1) MEDLINE 1966 to 1998: all hits for Echinac* screened.
Echinacea for preventing and treating the common cold (Review)

Methods of the review

Study identification:
Titles and - if available - abstracts of all references identified were screened by one reviewer (K.L.) who sorted out all which did not report on trials in humans including a control group. Copies of all other references were obtained and checked further for eligibility.

Assessing eligibility:
All identified controlled studies testing an Echinacea preparation in humans were checked for fulfillment of the selection criteria by three independent reviewers. Basic information (preparation tested, subjects included, type of control, design, reason for exclusion) of the trials excluded at that step was extracted. A total of 40 studies were assessed. There were four disagreements among the reviewers concerning eligibility; three were due to reading errors and could be easily resolved in discussion. The fourth was about a trial which did not state the method of allocation to treatment groups (Kleinschmidt 1965); as the description of this trial made it seem likely that allocation was quasi-randomized (alternation) it was finally decided to include this study.

Data extraction:
Descriptive information on patients, interventions, outcomes, results, drop-outs, and side effects was extracted by at least two independent reviewers using a standard form. Authors/manufacturers were contacted and asked to provide lacking and/or additional data. However, while we obtained some useful information regarding the general methods of some trials, lacking details (such as standard deviations, exact n for specific comparisons etc.) on results could not be collected with one exception (mostly because the trials were rather old and the data no longer fully available).

Details of the included studies are described in the table of included studies. The following abbreviations are used in the table:
comb = combination; E.pur = Echinacea purpurea, E.pal = Echinacea pallida, E.ang = Echinacea angustifolia - Methods (abbreviation A: method of allocation to groups; C: method of concealment of allocation; B: blinding; S: selection bias after allocation; Q: results of the quality scoring using the Jadad scale and our IV scale);
- Participants (N: number of patients randomized/analysed; P: condition/participants; D: demographic information; S: trial setting)
- Interventions (T: treatment group; C: control group);
- Outcomes (type and timing of outcomes);
- Notes: descriptive summary of results and remarks.

Assessment of quality of reports/methodological quality:
The quality of reports/methodological quality of included trials was assessed by at least two independent reviewers using - the method by Jadad et al. (Jadad 1996) (items on random allocation, blinding and reporting of drop-outs/exclusions adding to a summary score of 0 to 5 points);
- a scoring method developed by ourselves and used in published (Linde 1996a, Linde 1996b) and ongoing systematic reviews, the internal validity scale (IV scale). This instrument has 6 items (allocation to groups, concealment of allocation, baseline comparability, blinding of patients, blinding of evaluators, and likelihood of selection bias after allocation to groups by drop-out, etc.). Each item is scored between 0 (= criterion not met or insufficient information) and 1 (criterion met). The assessment of randomization concealment and double-blinding in this score system is equivalent to the method used by Schulz et al. (Schulz 1995).

For the calculation of scores only the information provided in the publications or written reports was used. The resulting quality scores are given in the table of included studies. For the informal description of quality features in that table we also used additional information gathered in personal communication from authors and sponsors.

Summarizing results:
We had decided in advance that a quantitative meta-analysis should be performed only under the following preconditions:
- preparations are comparable (from the same parts (e.g. roots) of the same plant species (e.g. E. purpurea) extracted in a similar way (e.g. ethanolic extraction))
- patients are comparable (similar definition of common cold/influenza-like syndromes)
- the methodology is similar (quality issues and outcome measurement).

Predefined main outcome measure for prevention trials was the number of patients with at least one episode of infection (results expressed as relative risk = proportion of patients with infection in the experimental group/proportion of patients with infection in the control group). Predefined outcome measures for treatment trials were duration and severity of infection.

Due to the heterogeneity of trials and insufficient reporting the summarizing of results proved to be difficult. For the prevention
studies we could extract data on numbers of participants with at least one infection. As the studied test preparations differed between the placebo-controlled trials we refrained from calculating a pooled effect size estimate. For a set of three studies comparing a combination of Echinacea with other plant extracts and no treatment, the above-mentioned preconditions were met. For the studies comparing Echinacea preparations and placebo in the treatment of common colds the preconditions were not met.

DESCRIPTION OF STUDIES

A total of 40 trials of preparations of Echinacea alone or in combinations with other plant extracts with a parallel control group were identified. 14 fully met the criteria for inclusion. One study made no explicit statement about the method of allocation to treatments; as this study was likely to have used alternation it was included (Kleinschmidt 1965). One study also investigated patients with suspected bacterial infection; as the majority of patients had a viral infection, however, and the results were presented separately for patients with suspected viral and bacterial infections, the trial was included (Bräunig 1993). The 16 included studies (involving 3396 patients) are summarized in the table of included studies. The remaining 24 studies did not meet the inclusion criteria (most often the reason for exclusion was either an indication other than common cold or non-random allocation; see table of excluded studies for details).

Based on clinical aspects we divided the 16 included studies into three categories:

- prevention trials with a placebo control (five trials with 1272 patients);
- prevention trials with a no treatment comparison (three trials with 1139 patients);
- treatment trials with a placebo control (eight trials with 985 patients).

Apart from two studies (Scaglione 1995, Hoheisel 1997) all were performed in Germany. Not a single trial was published in a Medline-listed journal.

1. Prevention trials with a placebo comparison

The five trials (Forth 1981, Hoheisel 1997, Melchart 1998, Schmidt 1990, Schöneberger 1992) in this category investigated a total of five different preparations in seven treatment groups (two trials - Forth 1981, and Melchart 1998 - were three-armed); two of the preparations were combinations and three were mono-preparations (E. purpurea herb, E. purpurea roots, E. angustifolia roots). In four of the trials participants took the study medication over a longer period (eight to 12 weeks) and the primary outcome measure was the number of patients with at least one infection. The remaining trial (Hoheisel 1997) differed considerably from the other four and has to be considered as a mixture of prevention and treatment trial. Workers in a furniture factory with a history of recurrent upper respiratory tract infection were asked to contact the factory physician in case of any first symptoms or feelings that they might be getting a cold. They then received either E. purpurea herb or placebo. Primary outcome measures were the number of patients developing a “full common cold” and the duration of illness.

2. Prevention trials with a no treatment comparison

In this category there are three relatively large trials (number of participants 209, 284 and 644) testing all a combination of Echinacea angustifolia and pallida roots, Baptisia tinctoria roots, Thuja occidentalis herb, and several homeopathic dilutions. The trials have been published 1961 (Helbig 1961), 1965 (Kleinschmidt 1965), and 1974 (Freyer 1974). All included children who were referred either to a pediatric in-patient department (for a variety of reasons, Helbig 1961) or for a stay in a health resort.

3. Treatment trials with a placebo control

The eight trials in this category investigated three different combinations and two mono-preparations. Inclusion diagnoses were “common cold” or “acute viral upper respiratory tract infection” in five trials, and more globally “upper respiratory tract infection” in three. While in two of these the description suggested that patients suffered from common colds, in one trial (Bräunig 1993) patients were classified according to suspected viral and bacterial origin. Treatment periods varied between six and ten days (as far as there was clear information). In most trials there seemed to be no predefined main outcome measures. Most frequently a catalogue of symptoms was scored at two control visits.

METHODOLOGICAL QUALITY

1. Prevention trials with a placebo comparison

Apart from one study with severe methodological flaws (Forth 1981; an unclear, but probably large number of patients have not been followed up and were excluded from the analysis) the studies in this category have acceptable methodological quality. All are randomized and double-blind, and major selection bias after allocation is unlikely. Fundamental problems of all trials are (1) the definition of common cold/upper respiratory tract infection and the reliability and validity of the clinical assessments made; and (2) limited sample size.

2. Prevention trials with no treatment controls

The three trials in this category cannot be considered to meet modern standards of good methodological quality. Allocation to the groups has not been truly randomized (alternate allocation explicitly described in Helbig 1961 and Freyer 1974, likely in Kleinschmidt 1965) and there was no blinding. In all three trials the operationalization of outcome measurement (definition of endpoints) was completely unclear. While there were no explicit descriptions of drop-outs and withdrawals the study approaches and conditions make it rather unlikely that there was a relevant loss to follow up.
3. Treatment trials with a placebo control
All eight trials in this category were randomized, and in all, apart from one trial which was single blind (Scaglione 1995), an attempt was made at double-blinding. In one three-armed study (Bräunig 1992a) comparing two different dosages of an Echinacea purpurea root extract and placebo, however, there is a severe flaw. All placebo patients received the low dosage; the high-dose group can, therefore, not be considered to be truly blind. Only one had a single clearly predefined main outcome measure.

Overall, the quality of reporting of most studies was insufficient. As a consequence, a reliable and valid assessment of the methodological quality of the trials was difficult. Some (Forth 1981, Freyer 1974, Helbig 1961, Kleinschmidt 1965, Bräunig 1992a) of the trials have severe shortcomings, and in some other reservations seem justified. Especially in the prevention trials where the medications have been taken over longer periods, it cannot be excluded that some unblinding might have happened as Echinacea extracts have a very characteristic taste. The method to conceal allocation has been described only in two study reports; for a number of other studies we could get information from authors or sponsors that neutrally packaged, consecutively numbered drugs were used. Drop-outs and withdrawals were described well in three trials only; in a number of reports the description suggested that there were no drop-outs or withdrawals but explicit statements were lacking. An intent to treat analysis was performed in three trials.

RESULTS

1. Prevention trials with a placebo comparison
Due to the heterogeneity of the five trials in this category, the calculation of a pooled effect size seemed not adequate. Two of the five trials (Forth 1981, Holheisel 1997) found a statistically significant lower incidence of infection in the treatment group (rate ratios 0.51 and 0.67) while in the other trials there were only trends in favour of the treatment groups (rate ratios 0.84, 0.86, 0.88). Results on severity and duration of infections were reported in three trials. There were no clear trends favouring the treatment or the placebo group regarding the severity of occurring infections. One trial (Holheisel 1997) found that the duration of illness was significantly shorter in the treatment group while in the two other trials (Melchart 1998, Schöneberger 1992) there were no marked differences.

The number of patients reporting adverse effects were given in four trials (none in both groups in the trial by Holheisel 1997; 18 of 100 patients in the E. angustifolia group, 10 of 99 in the E. purpurea group, and 11 of 90 in the placebo group in Melchart 1998; 12 of 322 in the treatment group and 10 of 324 in the placebo group in Melchart 1998; 7 of 54 in the treatment group and 11 of 54 in the placebo group in Schöneberger 1992).

2. Prevention trials with no treatment controls
In all three trials the number of children with infection was significantly lower in the group receiving the Echinacea combination compared to the no treatment group. The pooled rate ratio was 0.58 (0.42 to 0.81). There was no extractable data on other outcomes or side effects.

3. Treatment trials with a placebo control
Due to the insufficient presentation of results and the heterogeneity of outcome measures, data for a quantitative analysis could be extracted from only two trials for duration of illness, three trials for running nose, and from five trials (with a total of six treatment groups as one trial tested two dosages) when either duration, running nose or a summary symptom score was used (see analyses). The heterogeneity of the tested preparations precluded a pooled analysis. Overall, six trials claimed significantly positive results for the tested preparations over placebo (Bräunig 1992a for the high dose tested, Bräunig 1993, Reitz 1990, Scaglione 1995, Vorberg 1984, Vorberg 1989), one found significant results for a subgroup only (Henneicheke 1997), and two trials found no difference after treatment (Bräunig 1992a for the low dose tested, and Dorn 1989; in this trial, however, patients in the treatment group had more severe symptoms at baseline). Only three trials provided information on adverse events. In two (Dorn 1989, Scaglione 1995) there were no adverse effects and in one (Reitz 1990) four patients in the treatment group and five in the placebo group reported adverse effects.

DISCUSSION

The 16 controlled trials summarized in this review suggest that preparations containing extract of Echinacea probably can be effective in the prevention and treatment of common colds. Still, the evidence is far from compelling and conclusive for clinical decision making. The biggest problem is the great heterogeneity and the unclear comparability of the investigated products. A second relevant problem is that the quality of reporting is insufficient in about two thirds of the trials and raises doubts about the rigour. If the analyses were restricted to any single preparation or extract, it was not possible to perform conclusive quantitative meta-analyses.

The assessment of the evidence is further complicated by the fact that probably not all possibly relevant trials on the topic have been published. Until recently, herbal preparations have been assessed in Germany by a special commission (Commission E) at the Federal Drug Institute. This commission has licensed Echinacea purpurea herb and Echinacea pallida root while the evidence was judged as insufficient for other extracts (Dorsch 1996, Blumenthal 1998). The database on which the decisions are made is not fully transparent; it might be that positive studies exist which are not published for reasons of competition. We have personal information that a number (between five and ten) of unpublished trials of Echinacea preparations (at least partly on common cold) exist, probably in the majority with “negative” results.
AUTHORS’ CONCLUSIONS

Implications for practice

While overall there is some positive evidence, few recommendations can be made regarding the use of Echinacea products in practice. The heterogeneity of the available preparations and the limited quality and consistency of the evidence do not allow clear conclusions about which product might be effective in what dose and in what circumstances.

Patients and health care providers who want to use preparations containing extracts of Echinacea should be aware of the possible extreme differences in the chemical composition and that there is no solid base of evidence concerning their efficacy.

Cases of allergic reactions have been reported after parenteral use of Echinacea products (Schönhöfer 1989, Bauer 1996). As there is no evidence from controlled clinical trials that such parenteral administration is beneficial in the treatment and prevention of uncomplicated upper respiratory tract infections it should be discouraged. For oral intake the risks of serious adverse effects seem very small.

Implications for research

Given the widespread use of Echinacea products further research is clearly desirable. The use of chemically well-defined preparations is a precondition for the assessment of the comparability of results from different studies. There is ample space for improvement in the methodology and the reporting of clinical trials. The diagnostic classification of upper respiratory tract infections has to be more clearly defined in future studies. A single main outcome measure should be predefined for the confirmatory statistical analysis. The clinical assessment of the common cold is not easy; documentation instruments must not be too complicated (to warrant feasibility) but still should cover the relevant aspects of the course of the disease.

The available prevention studies suggest that any eventual prophylactic effect of Echinacea preparations might be relatively moderate in size (around 15 to 20% relative risk reduction). Studies to detect such differences have to have large sample sizes and are costly. At least in Germany, where most of the available studies have been performed, it seems questionable if such studies will be done. Most manufacturers of Echinacea products are relatively small and have only limited research expertise and budgets. As plant extracts cannot be patented easily the results of studies can be used by anyone else and do not provide marketing advantages.

In self-medication many people take Echinacea products when they experience the very first symptoms of a common cold and clearly before the illness has reached its maximum. Dosage is very high in the beginning and reduced after one or two days. This strategy is not easy to investigate in a normal general practice setting where patients seek doctor’s help only when the symptoms become burdening. The only study investigating this approach (Hoheisel 1997) yielded clearly positive results. In another recent study in which patients with a common cold were treated only the subgroup with recent onset of symptoms seemed to have a relevant benefit (Henneicke 1997). The treatment of early illness should therefore be preferred for research.

The informal information we got on publication bias is a major reason of concern. As long it is not guaranteed that all trials of Echinacea products will be published a question mark will remain on findings in systematic reviews on this topic.

NOTES

The Acute Respiratory Infections Group would like to thank Dr Bob Galloway, Ms Valerie Elder and Prof Malcolm Whyte for reading and commenting on this review.

POSSIBLE CONFLICT OF INTEREST

Dieter Melchart and Klaus Linde were involved in one of the studies included in this review.

SOURCES OF SUPPORT

External sources of support

- Karl und Veronica Carstens Foundation GERMANY
- NIAMS Grant No 5 U24-AR43346-02 USA
- Erich Rothenfußer Foundation GERMANY

Internal sources of support

- No sources of support supplied
References to studies included in this review

Bräunig 1992a (published and unpublished data)

Bräunig 1992b (published data only)

Bräunig 1993 (published and unpublished data)


Dorn 1989 (published and unpublished data)

Forth 1981 (published data only)

Freyer 1974 (published data only)

Hellig 1961 (published data only)

Hennecke 1997 (published data only)

Hoheisel 1997 (published data only)

Kleinschmidt 1965 (published data only)

Melchart 1998 (published data only)

Reitz 1990 (published and unpublished data)

Scaglione 1995 (published data only)

Schmidt 1990 (published data only)

Schönberger 1992 (published data only)

Vorberg 1984 (published data only)

Vorberg 1989 (published and unpublished data)

References to studies excluded from this review

Baetgen 1984

Baetgen 1988

Bendel 1989
Bendel R, Bendel V, Renner K, Carstens V, Stolze K. Additional treatment with Esberitox N in patients with chemo-radiotherapy

**Melchart 1995b**


**Melchart 1995c**

**Melchart 1995d**

**Melchart 1995c**

**Pohl 1970**

**Qadirpur 1976**

**Sartor 1972**

**Stolze 1986**

**Timmermanns 1990**

**Zimmer 1985**

### Additional references

**Bauer 1990**

**Bauer 1996**

**Blumenthal 1998**

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Characters of included studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Bräunig 1992a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>A: randomized (not explicitly stated in publication, information from the author)</td>
</tr>
<tr>
<td></td>
<td>C: numbered drugs</td>
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<tr>
<td></td>
<td>B: double-blinding stated but one group received a higher dose and was not truly double-blind</td>
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<tr>
<td></td>
<td>S: none (author confirmed in personal communication that there were no drop-outs and withdrawals, information in the publication was not fully clear)</td>
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<td></td>
<td>Q: Jadad 0-1-0, IV 0-0-0-5-0-5-0-0</td>
</tr>
<tr>
<td>Participants</td>
<td>N: 180/180</td>
</tr>
<tr>
<td></td>
<td>P: influenza-like URTI</td>
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<tr>
<td></td>
<td>D: ?</td>
</tr>
<tr>
<td></td>
<td>S: one general practice, Germany</td>
</tr>
<tr>
<td>Interventions</td>
<td>T1: Echinacea purpurea root extract 90 drops (450 mg) daily for 8 to 10 days</td>
</tr>
<tr>
<td></td>
<td>T2: Echinacea purpurea root extract 180 drops (900 mg) daily for 8 to 10 days</td>
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### Characteristics of included studies (Continued)

<table>
<thead>
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<th>Study Method</th>
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<th>Interventions</th>
<th>Outcomes</th>
<th>Notes</th>
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<tr>
<td><strong>Bräunig 1992b</strong></td>
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<tr>
<td>Methods</td>
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### Study Bräunig 1993

<table>
<thead>
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<th>Study Method</th>
<th>Participants</th>
<th>Interventions</th>
<th>Outcomes</th>
<th>Notes</th>
</tr>
</thead>
</table>
| Methods | A: randomized  
C: numbered drugs  
B: double  
S: report suggests that there were no drop-outs and withdrawals  
Q: Jadad 2-1-0, IV 1-1-0-0.5-1-0 | | | |
| Participants | N: 160?/160?  
P: upper respiratory tract infection (viral origin was suspected in 114 patients (70 vs. 44), bacterial in 46 (10 vs. 36))  
D: 48% female  
S: one general practice, Germany | | | |
| Interventions | | | | |
| Outcomes | | | | |
| Notes | | | | |

### Study Dorn 1989

<table>
<thead>
<tr>
<th>Study Method</th>
<th>Participants</th>
<th>Interventions</th>
<th>Outcomes</th>
<th>Notes</th>
</tr>
</thead>
</table>
| Methods | A: randomized  
C: consecutively numbered drugs  
B: double  
S: none  
Q: Jadad 1-1-1, IV 1-0-0-0.5-1-1 | | | | |
| Participants | N: 100/100  
P: acute infection of the upper respiratory tract  
D: 53% female, mean age 39 (treatment) and 35 (placebo) years  
S: ?, Germany | | | |

Both scores significantly better in group T2 (findings 2.7 +/- 2.2, symptoms 4.4 +/- 3.8) compared to T1 (findings 4.8 +/- 2.2, symptoms 10.1 +/- 3.5) and placebo (findings 5.1 +/- 2.0, symptoms 10.1 +/- 4.2).
### Characteristics of included studies (Continued)

| Interventions | T: combination 2 (Resistan containing mother tinctures of Echinacea angustifolia, Eupatorium perfoliatum, and Baptisia tinctoria) 30 ml on the first two days and 15 ml for the next four days  
|               | C: placebo |
| Outcomes     | Symptoms (tiredness, myalgia, headaches, running nose, cough, sore throat; assessed after two to four and six to eight days) |
| Notes        | Results (more reduction in the treatment group but no significant differences in symptom severity at the end of the study) difficult to interpret due to significant differences in the baseline severity of symptoms (more severe in the treatment group). |

### Allocation concealment

<table>
<thead>
<tr>
<th>Study</th>
<th>Forth 1981</th>
</tr>
</thead>
</table>
| Methods        | A: randomized  
|                | C: ?  
|                | B: partly blinded (two arms)  
|                | S: probably fatally flawed (an unclear, but probably large number of patients randomized dropped out and were not analyzed)  
|                | Q: Jadad 1-0-0, IV 1-0-0-0-0-0 |
| Participants   | N: ???/95  
|                | P: healthy volunteers  
|                | D: ?  
|                | S: industrial plant, Germany |
| Interventions  | T 1: combination 1 (Esberitox containing Echinacea angustifolia and pallida roots, Baptisia tinctoria roots, Thuja occidentalis herb, Apis D4, Crotalus D6, Silicea D4, Lachesis D6) as drops  
|                | T 2: combination 1 (same as above + 20 mg vitamine C) as tablets  
|                | C: Placebo (containing 20 mg vitamine C) tablets  
|                | Application: 3x25 drops (group 1) or 3x1 tablet daily for up to 16 weeks |
| Outcomes       | Number of patients who experienced a running nose |
| Notes          | Frequency of running nose 12/30 (group 1), 10/36 (group 2), 19/29 (placebo).  
|                | The number of patients randomized is not presented, but there is information that a large number of patients have been excluded from the analysis (drop-outs). Insufficient presentation, uninterpretable results |

### Allocation concealment

<table>
<thead>
<tr>
<th>Study</th>
<th>Freyer 1974</th>
</tr>
</thead>
</table>
| Methods        | A(llocation to groups): alternation (consecutive groups of about 35 children received either treatment or no treatment)  
|                | C(oncealment of randomization): none  
|                | B(linding): none  
|                | S(election bias after allocation): not reliably assessible but major bias seems unlikely  
|                | Q(uality scoring): Jadad 0-0-0, IV 0-0-0-0-0-0 |
| Participants   | N(umber of patients randomized/analyzed): 286/286  
|                | P(articipants and condition): children referred to a health resort for six weeks because of recurrent URTI  
|                | D(emographics): age 8 to 13 years  
|                | S(etting): health resort, Germany |
| Interventions  | T(reatment): combination 1 (Esberitox containing Echinacea angustifolia and pallida roots, Baptisia tinctoria roots, Thuja occidentalis herb, Apis D4, Crotalus D6, Silicea D4, Lachesis D6) 3x20 drops daily for 6 weeks  
|                | C(ontrol): no treatment |
| Outcomes       | Incidence of infections |
| Notes          | Proportion of children with at least one infection: Treatment group 69.5%, control group 49%. |
### Characteristics of included studies (Continued)

**Allocation concealment**

<table>
<thead>
<tr>
<th>Study</th>
<th>1971/72</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial performed</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Helbig 1961</td>
</tr>
</tbody>
</table>
| Methods                | A: alternation  
C: none  
B: none  
S: not reliably assessible but relevant bias seems unlikely  
Q: Jadad 0-0-0, IV 0-0-0-0-0-0 |
| Participants           | N: 644?/644?  
P: consecutive children admitted to a pediatric hospital (141 with serious infections treated with antibiotics, 308 with febrile infections not treated with antibiotics, 195 admitted for other reasons)  
D: age 1 to 3 years  
S: pediatric university hospital, Germany |
| Interventions          | T: combination 1 (Esberitox containing Echinacea angustifolia and pallida roots, Baptisia tinctoria roots, Thuja occidentalis herb, Apis D4, Crotalus D6, Silicea D4, Lachesis D6) 3x20 drops daily for 6 weeks  
C: no treatment |
| Outcomes               | Incidence of infections (among non-infected children) and of recurrences |
| Notes                  | Incidence of infections (among non-infected children): 15/95 in the treatment group and 36/100 in the control group. Recurrences: 50/222 vs. 100/227. Published 1961 |
| Allocation concealment | C |

### Study

<table>
<thead>
<tr>
<th>Study</th>
<th>Henneicke 1997</th>
</tr>
</thead>
</table>
| Methods                | A: randomized  
C: ?  
B: double  
S: none (intent to treat analysis)  
Quality scoring not done as full publication is not yet available |
| Participants           | N: 263/242  
P: common cold  
D: 63% female, age range 18 to 70 years  
S: 15 practices in Germany |
| Interventions          | T: combination 1 (Esberitox N containing Echinacea purpurea root, Baptisia tinctoria root, and Thuja occidentalis herb) for 7 to 9 days (dose unclear)  
C: placebo |
| Outcomes               | Main outcome measure: symptom score (O'Brien). Diary documenting 17 symptoms, clinical global impression index |
| Notes                  | Significant superiority of the treatment only in a (predefined) subgroup of patients treated in an early phase of the infection.  
Rigorous trial which is available as preliminary abstract and poster presentation only. Full report submitted - valid assessment possible only after publication |
| Allocation concealment | B |

### Study

<table>
<thead>
<tr>
<th>Study</th>
<th>Hoheisel 1997</th>
</tr>
</thead>
</table>
| Methods                | A: randomized  
C: ?  
B: double |

---

*Echinacea for preventing and treating the common cold (Review)*

Copyright © 2005 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd
<table>
<thead>
<tr>
<th>Study</th>
<th>Characteristics of included studies (Continued)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S: none</td>
</tr>
<tr>
<td></td>
<td>Q: Jadad 2-1-1, IV 1-0-1-0.5-1-1</td>
</tr>
<tr>
<td>Participants</td>
<td>N: 120/120</td>
</tr>
<tr>
<td></td>
<td>P: patients presenting with first symptoms of an URTI and having a history of recurrent URTI (&gt; 3 episodes in the previous 12 months)</td>
</tr>
<tr>
<td></td>
<td>D: 10% female, age 36.5 +/- 11 years</td>
</tr>
<tr>
<td></td>
<td>S: industrial plant in Sweden</td>
</tr>
<tr>
<td>Interventions</td>
<td>T: pressed juice of Echinacea purpurea herb, on day 1 every two hours 20 drops, then up to maximally 10 days 3x20 drops</td>
</tr>
<tr>
<td></td>
<td>C: placebo</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Primary outcome measures: number of patients who developed a “full” common cold and days until improvement. Secondary outcome measures: symptom diary, global assessments</td>
</tr>
<tr>
<td>Notes</td>
<td>Number of patients who developed a “full” common cold: 24/60 in the treatment group vs. 36/60 in the control group (p = 0.04). Patients in the treatment group experienced significantly earlier improvement (p &lt; 0.001)</td>
</tr>
<tr>
<td>Allocation concealment</td>
<td>B</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>Kleinschmidt 1965</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>A: unclear (alternation likely)</td>
</tr>
<tr>
<td></td>
<td>C: ?</td>
</tr>
<tr>
<td></td>
<td>B: none</td>
</tr>
<tr>
<td></td>
<td>S: not reliably assessible but major bias unlikely</td>
</tr>
<tr>
<td></td>
<td>Q: Jadad 0-0-0, IV 0-0-0-0-0-0</td>
</tr>
<tr>
<td>Participants</td>
<td>N: 209/209</td>
</tr>
<tr>
<td></td>
<td>P: children referred to a health resort for 6 weeks</td>
</tr>
<tr>
<td></td>
<td>D: age 3 to 5 years</td>
</tr>
<tr>
<td></td>
<td>S: health resort, Germany</td>
</tr>
<tr>
<td>Interventions</td>
<td>T: combination 1 (Esberitox containing Echinacea angustifolia and pallida roots, Baptisia tinctoria roots, Thuja occidentalis herb, Apis D4, Crotalus D6, Silicea D4, Lachesis D6) 3x1 tablet daily for 6 weeks</td>
</tr>
<tr>
<td></td>
<td>C: no treatment</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Number of children with infections, days with fever</td>
</tr>
<tr>
<td>Notes</td>
<td>57% of treated children had an infection compared to 78% in the untreated group. Duration of fever was 3.8 days in the treatment group vs. 4.4 days in the untreated group. Published 1965</td>
</tr>
<tr>
<td>Allocation concealment</td>
<td>C</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>Melchart 1998</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>A: randomized</td>
</tr>
<tr>
<td></td>
<td>C: consecutively numbered drugs</td>
</tr>
<tr>
<td></td>
<td>B: double</td>
</tr>
<tr>
<td></td>
<td>S: unlikely (intent to treat and per protocol analysis)</td>
</tr>
<tr>
<td></td>
<td>Q: Jadad 2-1-1, IV 1-1-1-0.5-1-1</td>
</tr>
<tr>
<td>Participants</td>
<td>N: 302/289, 214 complied fully with the protocol</td>
</tr>
<tr>
<td></td>
<td>P: healthy volunteers</td>
</tr>
<tr>
<td></td>
<td>D: 29% female, mean age 29.5 +/- 10.4 years</td>
</tr>
<tr>
<td></td>
<td>S: 5 centers (4 military centers, 1 industrial plant) were randomized; 289 participants were analyzed intent to treat</td>
</tr>
<tr>
<td>Interventions</td>
<td>T 1: Echinacea angustifolia root extract</td>
</tr>
</tbody>
</table>

Echinacea for preventing and treating the common cold (Review)

Copyright © 2005 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd
**Characteristics of included studies (Continued)**

T 2: Echinacea purpurea root extract  
C: placebo (coloured ethanolic solution)  
Application and dosage: 2x50 drops daily from Monday to Friday for 12 weeks

**Outcomes**  
Predefined main outcome measure: time until occurrence of first URTI.  
Secondary outcomes: proportions with at least one URTI; number, severity and duration of episodes, global assessment. Predefined subgroup analysis on patients with more than 3 infections in the previous 12 months

**Notes**  
Time to first infection 66 days (95%CI 61-72, group 1), 69 (64-74, group 2), and 65 days (59-70, placebo, p = 0.49). Proportions with at least one infection in group 1: 32% (23-41%), group 2: 29% (20-38%), placebo: 37% (27-47%). Global assessment better in the experimental groups (p = 0.04); more volunteers in treatment groups correctly guessed that they had received a true treatment (p < 0.001; unblinding?).

**Allocation concealment A**

<table>
<thead>
<tr>
<th>Study</th>
<th>Reitz 1990</th>
</tr>
</thead>
</table>
| Methods | A: randomized  
C: ?  
B: double  
S: relevant bias unlikely  
Q: Jadad 1-1-0, IV 1-0-0-0.5-1-0.5 |
| Participants | N: 150/139  
P: patients with viral upper respiratory tract infection and a history of recurrent infections  
D: 21% female, mean age 38 (treatment) and 43 (control) years  
S: police department in German city |
| Interventions | T: combination 1 (Esberitox N containing Echinacea purpurea root, Baptisia tinctoria root, and Thuja occidentalis herb) 3x3 tablets daily for two months  
C: placebo (containing vitamin C) |
| Outcomes | Symptoms (assessed after seven and 14 days), immunological analyses and recurrence |
| Notes | Symptoms in the treatment group attenuated more rapidly (difference for some symptoms significant), 4 recurrences in the treatment group vs. 6 in the control group.  
Apparently rigorous but insufficiently reported study |

**Allocation concealment B**

<table>
<thead>
<tr>
<th>Study</th>
<th>Scaglione 1995</th>
</tr>
</thead>
</table>
| Methods | A: randomized  
C: ?  
B: single  
S: ?  
Q: Jadad 1-0-0, IV 1-0-0-0.5-0-0 |
| Participants | N: 32/32?  
P: common cold  
D: 47% female, age range 18 to 71 years  
S: ?, Italy |
| Interventions | T: combination 3 (containing Echinacea purpurea root extract (25 mg); vitamine C 100 mg; rosemary leaf extract (20.1 mg); eucalyptus leaf extract (12.3 mg); fennel seed extract (10.3 mg)) 4 tablets daily  
C: placebo |
| Outcomes | Duration of illness based on rhinorrea and the number of paper tissues used daily for each subject |
| Notes | Duration of illness 3.4 +/- 1.2 days in the treatment group vs. 4.37 +/- 1.57 days in the placebo group (p < 0.01). Number of paper tissues lower in the treatment group. |
### Characteristics of included studies (Continued)

Straightforward trial with a number of reporting deficiencies

<table>
<thead>
<tr>
<th>Allocation concealment</th>
<th>Study</th>
<th>Schmidt 1990</th>
</tr>
</thead>
</table>
|                         | Methods | A: randomized (not explicitly stated in the publication but information from authors)  
C: ?  
B: double  
S: major bias unlikely in spite of per protocol analysis  
Q: Jadad 0-1-1, IV 0-0-1-0.5-1-0.5 |
|                         | Participants | N: 646/609  
P: university students  
D: 37% female, age 10 to 31 years  
S: research institute, Germany |
|                         | Interventions | T: combination 2 (Resistan containing mother tinctures of Echinacea angustifolia, Eupatorium perfoliatum, and Baptisia tinctoria) once daily 12 ml for 8 weeks  
C: placebo |
|                         | Outcomes | Incidence of infections, symptom monitoring in case of infections |
|                         | Notes | Incidence of at least one infection: 41% treatment group, 48% placebo group (p = 0.08). Incidence of at least one infection in volunteers with > 3 infections in the previous 12 months: 47% treatment group, 58% placebo group; no results on severity presented |
| Allocation concealment | Study | Schöneberger 1992 |
| B                      | Methods | A: randomized  
C: ?  
B: double  
S: none  
Q: Jadad 1-1-1, IV 1-0-1-0.5-0.5-1 |
|                         | Participants | N: 109/108  
P: volunteers with more than 3 URTIs in the previous 6 months of winter  
D: 62% female, age 13-84 years  
S: general practice, Germany |
|                         | Interventions | T: pressed juice of Echinacea purpurea herb, 2x4 ml daily for 8 weeks  
C: placebo |
|                         | Outcomes | Incidence, number, severity, and duration of infections; time to first infection, CD4/CD8-ratio |
|                         | Notes | Incidence: 65% (treatment), 74% (placebo); number of infections: 42 vs. 50; more severe infections: 8 vs. 16; time to first infection: 40 vs. 25 days; duration: 7.4 vs. 7.1 days |
| Allocation concealment | Study | Vorberg 1984 |
| B                      | Methods | A: randomized  
C: ?  
B: double  
S: major bias unlikely  
Q: Jadad 1-1-1, IV 1-0-0-0.5-1-0.5 |
|                         | Participants | N: 100/90  
P: common cold |
D: 54% female, age 18 to 60 years
S: ?, Germany

Interventions
T: combination 1 (Esberitox containing Echinacea angustifolia and pallida roots, Baptisia tinctoria roots, Thuja occidentalis herb, Apis D4, Crotalus D6, Silicea D4, Laeasis D6) three times daily two tablets
C: placebo (containing vitamin C)

Outcomes
10 symptoms (assessed after three and ten days)

Notes
Most symptoms significantly better in the treatment group after three days. Both groups almost symptom free after ten days.
Insufficient presentation of results.

Allocation concealment
B

Study
Vorberg 1989

Methods
A: randomized
C: consecutively numbered drugs
B: double
S: possible
Q: Jadad 1-1-0, IV 1-0-0-0.5-1-0

Participants
N: 100/81
P: upper respiratory tract infection
D: 57% female, mean age 43 +/- 11 years
S: ?, Germany

Interventions
T: combination 2 (Resistan containing mother tinctures of Echinacea angustifolia, Eupatorium perfoliatum, and Baptisia tinctoria) 30 ml daily for the first two days and 15 ml for further four days
C: placebo

Outcomes
Nine symptoms (assessed after two to three and eight to ten days)

Notes
Seven of nine symptoms significantly better in the treatment group after two to three days, and eight of nine after eight to ten days

Allocation concealment
A

Characteristics of excluded studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baetgen 1984</td>
<td>Not randomized</td>
</tr>
<tr>
<td></td>
<td>Not common cold (pertussis)</td>
</tr>
<tr>
<td>Baetgen 1988</td>
<td>Not randomized</td>
</tr>
<tr>
<td></td>
<td>Not common cold (acute bronchitis)</td>
</tr>
<tr>
<td>Bendel 1989</td>
<td>Not common cold (reduction of immunosuppressive side effects of combined radio-chemotherapy in patients with breast cancer)</td>
</tr>
<tr>
<td>Bendel 1990</td>
<td>Not common cold (reduction of immunosuppressive side effects of radiotherapy in patients with breast cancer)</td>
</tr>
<tr>
<td>Blumröder 1985</td>
<td>Not common cold (angina lacunaris)</td>
</tr>
<tr>
<td>Coeugniert 1986</td>
<td>Not randomized</td>
</tr>
<tr>
<td></td>
<td>Not common cold (recurrent vaginal candida infection)</td>
</tr>
<tr>
<td>Cubasch 1992</td>
<td>Only measurement of laboratory and psychological parameters</td>
</tr>
<tr>
<td>Ehringer 1968</td>
<td>Not common cold (venous insufficiency)</td>
</tr>
<tr>
<td>Engel 1988</td>
<td>Not randomized</td>
</tr>
</tbody>
</table>
Characteristics of excluded studies (Continued)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Reason for Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freitag 1984</td>
<td>Not common cold (pertussis)</td>
</tr>
<tr>
<td>Hill 1993</td>
<td>Not common cold (topical treatment of insect bites)</td>
</tr>
<tr>
<td>Hill 1995</td>
<td>Not common cold (topical treatment of insect bites)</td>
</tr>
<tr>
<td>Hill 1996</td>
<td>Not common cold (topical treatment of insect bites)</td>
</tr>
<tr>
<td>Melchart 1995a</td>
<td>Measurement of immunological parameters in healthy volunteers</td>
</tr>
<tr>
<td>Melchart 1995b</td>
<td>Measurement of immunological parameters in healthy volunteers</td>
</tr>
<tr>
<td>Melchart 1995c</td>
<td>Measurement of immunological parameters in healthy volunteers</td>
</tr>
<tr>
<td>Melchart 1995d</td>
<td>Measurement of immunological parameters in healthy volunteers</td>
</tr>
<tr>
<td>Melchart 1995e</td>
<td>Measurement of immunological parameters in healthy volunteers</td>
</tr>
<tr>
<td>Pohl 1970</td>
<td>Not randomized, Not common cold (reduction of radiotherapy-induced leukopenia)</td>
</tr>
<tr>
<td>Qadripar 1976</td>
<td>Not common cold (skin infections)</td>
</tr>
<tr>
<td>Sartor 1972</td>
<td>Not common cold (reduction of radiotherapy-induced leukopenia)</td>
</tr>
<tr>
<td>Stolze 1986</td>
<td>Not randomized, Not common cold (variety of respiratory tract infections treated with antibiotics)</td>
</tr>
<tr>
<td>Timmermanns 1990</td>
<td>Not common cold (urinary disfunction)</td>
</tr>
<tr>
<td>Zimmer 1985</td>
<td>Not common cold (acute sinusitis)</td>
</tr>
</tbody>
</table>

**Graphs**

Comparison 01. Echinacea vs. placebo to prevent common cold

<table>
<thead>
<tr>
<th>Outcome title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Number of participants with at least one infection episode</td>
<td></td>
<td></td>
<td>Peto Odds Ratio 95% CI</td>
<td>Totals not selected</td>
</tr>
</tbody>
</table>

Comparison 02. Echinacea vs. no treatment to prevent common cold

<table>
<thead>
<tr>
<th>Outcome title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Number of participants with at least one infection episode</td>
<td></td>
<td></td>
<td>Peto Odds Ratio 95% CI</td>
<td>Subtotals only</td>
</tr>
</tbody>
</table>

Comparison 03. Echinacea vs. placebo to treat patients with common cold

<table>
<thead>
<tr>
<th>Outcome title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Preference outcome: 1) duration of illness; 2) symptom scores; 3) running nose</td>
<td></td>
<td></td>
<td>Weighted Mean Difference (Fixed) 95% CI</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>02 Running nose</td>
<td></td>
<td></td>
<td>Weighted Mean Difference (Fixed) 95% CI</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>03 Duration of illness</td>
<td></td>
<td></td>
<td>Weighted Mean Difference (Fixed) 95% CI</td>
<td>Totals not selected</td>
</tr>
</tbody>
</table>

**Index Terms**

Medical Subject Headings (MeSH)

Common Cold [*prevention & control; *therapy]; Echinacea [*therapeutic use]; Phytotherapy; Plant Extracts [*therapeutic use]; *Plants, Medicinal
Echinacea for preventing and treating the common cold

MeSH check words
Humans

COVER SHEET

Title
Echinacea for preventing and treating the common cold

Authors
Melchart D, Linde K, Fischer P, Kaesmayr J

Contribution of author(s)
Information not supplied by author

Issue protocol first published
1997/4

Review first published
1999/1

Date of most recent amendment
17 February 2005

Date of most recent SUBSTANTIVE amendment
18 November 1998

What's New
Information not supplied by author

Date new studies sought but none found
Information not supplied by author

Date new studies found but not yet included/excluded
Information not supplied by author

Date new studies found and included/excluded
Information not supplied by author

Date authors' conclusions section amended
Information not supplied by author

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DOI
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CD000530

Editorial group
Cochrane Acute Respiratory Infections Group

Editorial group code
HM-ARI

COMMENTS AND CRITICISMS

Duration of echinacea dosage

Summary
I wish to comment on the Cochrane review "Echinacea for preventing and treating the common cold". It is claimed in the Hot Topic of the Month (Relief from coughs & colds), August 2001, p5, para. 6.1, that “the German drug regulatory authority recommends that it be used for no longer than eight weeks at a time”. I have asked the Consumer Network about the evidence for this and been told that it is not available. Nevertheless, I think that if it is indeed a recommendation of the German drug regulatory authority, it should be mentioned in both the review and the abstract.

I certify that I have no affiliations with or involvement in any organisation or entity with a direct financial interest in the subject matter of my criticisms.

Author’s reply
Contributors
David Potter

**GRAPHS AND OTHER TABLES**

**Comparison 03.  01 Number of participants with at least one infection episode**

<table>
<thead>
<tr>
<th>Study</th>
<th>Echinacea n/N</th>
<th>Placebo n/N</th>
<th>Peto Odds Ratio 95% CI</th>
<th>Peto Odds Ratio 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 mono-preparations</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hoheisel 1997</td>
<td>24/60</td>
<td>36/60</td>
<td></td>
<td>0.45 [0.22, 0.92]</td>
</tr>
<tr>
<td>Melchart 1998</td>
<td>61/199</td>
<td>33/90</td>
<td></td>
<td>0.76 [0.45, 1.29]</td>
</tr>
<tr>
<td>Schneberger 1992</td>
<td>35/54</td>
<td>40/54</td>
<td></td>
<td>0.65 [0.29, 1.47]</td>
</tr>
<tr>
<td>02 combinations</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Forth 1981</td>
<td>22/66</td>
<td>19/29</td>
<td></td>
<td>0.27 [0.11, 0.66]</td>
</tr>
<tr>
<td>Schmidt 1990</td>
<td>132/322</td>
<td>155/324</td>
<td></td>
<td>0.76 [0.56, 1.03]</td>
</tr>
</tbody>
</table>
### Comparison 03. 01 Number of participants with at least one infection episode

**Review:** Echinacea for preventing and treating the common cold

**Comparison:** 02 Echinacea vs. no treatment to prevent common cold

**Outcome:** 01 Number of participants with at least one infection episode

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Control</th>
<th>Peto Odds Ratio</th>
<th>Weight</th>
<th>Peto Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>95% CI (%)</td>
<td>(%)</td>
<td>95% CI</td>
</tr>
<tr>
<td>01 mono-preparations</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events:</td>
<td>0 (Treatment), 0 (Control)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: not applicable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>02 combinations</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Freyer 1974</td>
<td>43/140</td>
<td>74/144</td>
<td></td>
<td>27.2</td>
<td>0.43 [ 0.27, 0.68 ]</td>
</tr>
<tr>
<td>Helbig 1961</td>
<td>62/322</td>
<td>140/322</td>
<td></td>
<td>54.6</td>
<td>0.33 [ 0.23, 0.45 ]</td>
</tr>
<tr>
<td>Kleinschmidt 1965</td>
<td>62/109</td>
<td>78/100</td>
<td></td>
<td>18.2</td>
<td>0.39 [ 0.22, 0.69 ]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>571</td>
<td>566</td>
<td></td>
<td>100.0</td>
<td>0.36 [ 0.28, 0.46 ]</td>
</tr>
<tr>
<td>Total events:</td>
<td>167 (Treatment), 292 (Control)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity chi-square=0.92 df=2 p=0.63 I =0.0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect z=8.11  p&lt;0.00001</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Comparison 03. 01 Preference outcome: 1) duration of illness; 2) symptom scores; 3) running nose

**Review:** Echinacea for preventing and treating the common cold

**Comparison:** 03 Echinacea vs. placebo to treat patients with common cold

**Outcome:** 01 Preference outcome: 1) duration of illness; 2) symptom scores; 3) running nose

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Control</th>
<th>Weighted Mean Difference (Fixed)</th>
<th>Weighted Mean Difference (Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)</td>
<td>N</td>
<td>Mean(SD)</td>
</tr>
<tr>
<td>01 mono-preparations</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brunig 1992a</td>
<td>60</td>
<td>10.10 (3.50)</td>
<td>60</td>
<td>10.10 (4.20)</td>
</tr>
<tr>
<td>Brunig 1992b</td>
<td>60</td>
<td>4.40 (3.80)</td>
<td>60</td>
<td>10.10 (4.20)</td>
</tr>
<tr>
<td>Brunig 1993</td>
<td>70</td>
<td>9.10 (1.80)</td>
<td>44</td>
<td>12.90 (2.10)</td>
</tr>
<tr>
<td>02 combinations</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dorn 1989</td>
<td>50</td>
<td>1.44 (0.73)</td>
<td>50</td>
<td>1.42 (0.71)</td>
</tr>
<tr>
<td>Scaglione 1995</td>
<td>16</td>
<td>3.37 (1.25)</td>
<td>16</td>
<td>4.37 (1.57)</td>
</tr>
<tr>
<td>Vorberg 1984</td>
<td>37</td>
<td>0.41 (0.55)</td>
<td>44</td>
<td>1.06 (0.73)</td>
</tr>
</tbody>
</table>
### Comparison 03. 02 Running nose

Review: Echinacea for preventing and treating the common cold  
Comparison: 03 Echinacea vs. placebo to treat patients with common cold  
Outcome: 02 Running nose  

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Control</th>
<th>Weighted Mean Difference (Fixed)</th>
<th>Weighted Mean Difference (Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N Mean(SD)</td>
<td>N Mean(SD)</td>
<td>95% CI</td>
<td>95% CI</td>
</tr>
<tr>
<td>01 mono-preparations</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brunig 1992a</td>
<td>60 1.30 (0.50)</td>
<td>60 1.30 (0.60)</td>
<td>0.00 [-0.20, 0.20]</td>
<td></td>
</tr>
<tr>
<td>Brunig 1992b</td>
<td>60 0.80 (0.60)</td>
<td>60 1.30 (0.60)</td>
<td>-0.50 [-0.71, -0.29]</td>
<td></td>
</tr>
<tr>
<td>02 combinations</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dorn 1989</td>
<td>50 1.44 (0.73)</td>
<td>50 1.42 (0.71)</td>
<td>0.02 [-0.26, 0.30]</td>
<td></td>
</tr>
<tr>
<td>Vorberg 1984</td>
<td>37 0.41 (0.55)</td>
<td>44 1.06 (0.72)</td>
<td>-0.65 [-0.93, -0.37]</td>
<td></td>
</tr>
</tbody>
</table>

### Comparison 03. 03 Duration of illness

Review: Echinacea for preventing and treating the common cold  
Comparison: 03 Echinacea vs. placebo to treat patients with common cold  
Outcome: 03 Duration of illness  

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Control</th>
<th>Weighted Mean Difference (Fixed)</th>
<th>Weighted Mean Difference (Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N Mean(SD)</td>
<td>N Mean(SD)</td>
<td>95% CI</td>
<td>95% CI</td>
</tr>
<tr>
<td>01 mono-preparations</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brunig 1993</td>
<td>70 9.10 (1.80)</td>
<td>44 12.90 (2.10)</td>
<td>-3.80 [-4.55, -3.05]</td>
<td></td>
</tr>
<tr>
<td>02 combinations</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scaglione 1995</td>
<td>16 3.37 (1.25)</td>
<td>16 4.37 (1.57)</td>
<td>-1.00 [-1.98, -0.02]</td>
<td></td>
</tr>
</tbody>
</table>