Echinacea:

Primary:

1. **Schapowal A, Berger D, Klein P, Suter A. Echinacea/sage or chlorhexidine/lidocaine for treating acute sore throats: A randomized double-blind trial. Eur J Med Res 2009; 14: 406-412.**

Extended Abstract:

Study Objectives: The aim of the trial was to assess the relative efficacy of a herbal Echinacea/sage spray to a chlorhexidine/lidocaine spray in the treatment of acute sore throats.

Methods:

- Design: Multicenter, randomized, double-blind, double-dummy controlled trial.
- Allocation: A total of 154 patients were screened, randomized and treated. A total of 80 patients were allocated to the echinacea/sage group and 74 to the chlorhexidine/lidocaine group. The baseline characteristics between treatment groups were comparable, with the only significant difference found for age were those patients allocated to the chlorhexidine/lidocaine group seemed to be younger. Furthermore, the throat score as determined by the tonsillopharyngitis severity score was found to be somewhat higher at baseline for patient allocated to the chlorhexidine/lidocaine treatment group.
- Blinding: double-blind, double-dummy controlled trial.
- Follow-up Period: 5 days following the onset of sore throat symptoms. The average study duration was 5.6 days for the echinacea/sage group and 6.4 days for the chlorhexidine/lidocaine group.
- Participants: A total of 154 patients were recruited from 11 different general physician practices in Switzerland. All patients were at least 12 years old with acute sore throat (i.e. acute pharyngitis or tonsillitis with symptoms of pain and inflammation of the pharynx and/or tonsils) present for not more than 72 hours prior to study inclusion with a tonsillopharyngitis severity score of 6 or greater. Patients were excluded from the study if they had recently used analgesics, antibiotics, topical throat pain medication or systemic corticosteroids. Additional exclusion criteria were symptoms of a bacterial pharyngitis infection, allergy to of the study herbs, pregnancy or lactation, hypersensitivity to ibuprofen or recent participation in a previous clinical trial.
- Intervention: Patients received either a 50 mL Echinacea/sage throat spray containing an aqueous alcohol fresh-plant extract of *Echinacea purpurea* (95% aerial parts and 5% root) and leaves tincture of *Salvia officinalis* or a commercial throat spray containing 1% chlorhexidine gluconate and 2% lidocaine hydrochloride. Regardless of which treatment group patients were assigned to, both sprays were administered as two sprays every 2 hours up to 10 times daily until they were symptom-free, for a maximum of 5 days. Owing to the fact it was a double-dummy blinded study, in addition to receiving a treatment spray each patient also received a placebo spray that was similar in appearance, taste and smell to other treatment spray they did not receive. The treatment and placebo sprays were issued to patients in a sealed box together with 20 tablets of ibuprofen 200 mg hat served as a rescue medication if the pain symptoms became too severe.
- Outcomes: The primary study outcome was to compare the patient response rates to the Echinacea/sage throat spray to those obtained for the chlorhexidine/lidocaine spray during the first 3 days of use. The patient response to the treatment was assessed at baseline and during treatment by the patient using a tonsillopharyngitis symptom severity score which consisted of ratings for symptoms of throat pain, difficulty swallowing, salivation, erythema and fever. A

response to treatment was defined as a decrease of at least 50% of the total baseline symptom score taken prior to treatment.

- Patient Follow-up: Treatment duration was until illness resolution or for a maximum of 5 consecutive days. Although 154 patient were screened, randomized and treatment, 21 patient were either excluded secondary to incorrect use of the study medications or were lost to follow-up. Therefore, a total of 133 patients were included as part of the study. To check blinding at the end of the treatment, patient were asked to guess which bottle contained the treatment. Compliance was checked by weighting the returned bottles and counting the number of rescue ibuprofen used and patients documented in a dairy how many times they had applied each spray daily.
- Setting: Outpatient, multicenter, general physician practice, community trial in Switzerland.

Main Results: The Echinacea/sage treatment spray exhibited similar efficacy to the chlorhexidine/lidocaine treatment spray in reducing sore throat symptoms during the first 3 days following use and for each day of use. Response rates after 3 days were reported as 63.8% in the echinacea/sage group and 57.8% in the chlorhexidine/lidocaine group. The response rates for day 4 were 69.6% for echinacea/sage and 70.3% for chlorhexidine/lidocaine, respectively, and for day 5, they were 73.9% and 79.7. The time point at which 50% of patients in the Echinacea/sage treatment group were symptom-free (total tonsillopharyngitis symptom severity score ≤ 2) was the evening of day 4, while 50% of patients in the chlorhexidine/lidocaine group achieved symptom-free status the morning of day 5. At day 5, 50.7% of the patients allocated to the Echinacea/sage treatment group and 56.7% of patients allocated to the chlorhexidine/lidocaine treatment group were assessed to be symptom-free. Both treatments were very well tolerated by study participants. Investigators rated the efficacy as very good or good in 88.4% of patients using the echinacea/sage spray and in 89.1% of all patients using the chlorhexidine/lidocaine spray. Patients' efficacy ratings were similar, with "very good" or "good" in 89.9% of the echinacea/sage and 89.1% of the chlorhexidine/lidocaine cases.

Conclusions: An echinacea/sage spray preparation is as efficacious and well tolerated as chlorhexidine/lidocaine spray in the treatment of acute sore throats.

Comments/Critical Appraisal (including assessment of internal and external validity):

A major limitation of this study was its small sample size and that despite randomization, there was some variability in term baseline throat symptom severity between treatment groups as study patients allocated to the chlorhexidine/lidocaine treatment group reported has having a higher throat score compared to those allocated to the Echinacea/sage treatment group. Furthermore, given that Echinacea and sage were administered and studied together, it is difficult to elucidate whether the efficacy demonstrated by this study was attributed to the Echinacea, the sage or the combination of both being administered together. The internal validity of the study is strong since investigators randomized, double-blinded and double-dummied the study, assessed for blinding during the study, accounted for compliance as well as performed objective physician assessments at baseline and following treatment completion. The subjective nature of the patient throat symptom severity scoring system used by the study investigators to assess efficacy supports the study's internal validity although it is unknown whether the scoring system itself is validated. The strict inclusion and exclusion criterion strengthens the study's internal validity but weakens its external validity. The study is externally valid only for patients who meet the inclusion/exclusion criteria limiting the number of patient eligible to use an Echinacea/sage throat spray. One last thing that may call into question the internal and external validity of the study is the fact that it was sponsored by A. Vogel Bioforce AG, the manufacturers of the

Echinacea/sage herbal throat spray utilized as part of this study. Considering this, results obtained may be bias and further investigation is required in order to confirm or refute this. However, subsequent investigations of Echinacea throat sprays and its efficacy are limited. In terms of external validity, the fact that A. Vogel Bioforce AG sponsored the investigation does strength its external validity since a very similar herbal throat spray to the one utilized in the study, specifically the A.Vogel Sore Throat Spray, is readily available in Canada for patients to use.

2. Goel V, Lovlin R, Barton R, Lyon MR, Bauer R, Lee TD, Basu TK. Efficacy of a standardized echinacea preparation (Echinilin) for the treatment of the common cold: a randomized, double-blind, placebo-controlled trial. J Clin Pharm Ther. 2004 Feb;29(1):75-83.

Extended Abstract:
Study Objectives: The aim of this study was to test the clinical efficacy of the highly standardized *Echinacea purpurea* formulation, specifically Echinilin, in decreasing the severity and duration of symptoms associated with a naturally acquired common cold.

Methods:
- Design: A randomized, double-blind, placebo-controlled trial
- Allocation: A total of 282 volunteers, aged 18 to 65 years with a history of two or more colds in the previous year, but otherwise in good health, were recruited for the study. Patients were then randomized to receive either echinacea or placebo and given instructions to start taking the designated treatment at the onset of the first symptom related to a cold. Of the 282 volunteers, 128 contracted a common cold, 59 received echinacea and 69 placebo. The groups were virtually identical with respect to age, smoking status and history of past colds except for the ratio of males to females.
- Blinding: double-blind, randomized control trial.
- Follow-up Period: 7 days following the onset of cold symptom(s).
- Participants: A total of 282 volunteers, aged 18 to 65 years with a history of two or more colds in the previous year, but otherwise in good health, were recruited for the study. Subjects were excluded if they had been vaccinated against influenza in the past 6 months, were allergic to ragweed, had multiple sclerosis, tuberculosis, diabetes, cancer, lupus, asthma, fibromyalgia, HIV/AIDS or cardiovascular disease, or were on immunosuppressive drugs such as corticosteroids or cyclosporine. Pregnant and lactating women were also excluded.
- Intervention: Patients were assigned to take either echinacea or placebo as treatment at the onset of the first symptom of the first symptom related to a common cold. Cold symptoms for the purpose of this investigation included sore throat, runny nose, watery eyes, chills, malaise, fever, headache, sore muscles hoarseness, shortness of breath and cough. Subjects were instructed not to take any other medication for these symptoms during the treatment. Treatment with consisted of 10 doses of either echinacea or placebo, depending on which the patient was assigned, taken on the first day, distributed equally throughout the day, followed by four doses per day for the next 6 days. Echinacea and placebo treatments were both liquid dosage forms and a dose was measure to be 4 mL of formulation diluted with a half glass of water.
- Outcomes: The primary efficacy end point was the change in Total Daily Symptom Scores (TDSS) for the 7-day treatment period. To explain, participants were asked to complete a daily self-assessment log documenting the severity of their cold symptoms for the 7-day evaluation period. The self-assessment was determined on a 10-point scale as follows, 0 = no symptom, 1–3 = a mild symptom, 4–6 = a moderate symptom, and 7–9 = a severe symptom. Each of the

following symptoms were assessed; sore throat, runny nose, watery eyes, chills, malaise, fever, headache, sore muscles hoarseness, shortness of breath and cough. TDSS were calculated by summing the daily scores for all the symptoms.

- Patient Follow-up: Patients were followed up with after their 7 day treatment period. In addition to self-assessment of cold symptoms, study participants were also required to see a nurse, trained by the study physician, to have the severity of their cold symptoms assessed by visual and physical assessment. At the same time, the nurse also examined the subjects for possible evidence of secondary complications and collected fasting blood samples to allow for the determination of white blood cell differential counts. The secondary efficacy parameters were the change in total symptom scores (overall mean) for the specific symptoms, duration of specific symptoms (number of days for which the total score was >3, i.e., moderate to severe), and response rate to the treatments. Response rate refers to the percentage of subjects demonstrating at least a 50% reduction in their maximum TDSS.
- Setting: Outpatient, Community-based controlled trial in Edmonton, Alberta, Canada.

Main Results: Overall, the study results demonstrated that early intervention with a standardized preparation of echinacea (Echinilin) was associated with a statistically significant decrease in the average severity and duration of common cold symptoms. More specifically, of the 128 patients who actually developed symptoms of the common cold, those patients taking echinacea were found to possess significantly lower self-assessed TDSS throughout the treatment duration. Specifically looking at the overall mean symptom severity scores for sore throat, it was found to be 39% lower in the echinacea group compared to those taking placebo. Similar results were obtained from assessments made by the study nurse. In terms of response rates, investigators found that 50% of subjects in the echinacea group showed at least a 50% reduction in their maximal TDSS by day 4 of treatment. In comparison, this same effect was found not to occur until after approximately 5.5 days in those patients taking placebo. The duration of all common cold symptoms, excluding cough, was also found to be approximately 27% (or 1.5 days) shorter in those patient treated with echinacea compared to placebo. Specifically for sore throat, echinacea was shown to statistically significantly reduce the duration of this symptom by 0.7 of a day compared to placebo. Overall, echinacea was well tolerated by the study participants.

Conclusions: Early intervention with a standardized formulation of echinacea (Echinilin) was well tolerated and efficacious in reducing symptom severity in subjects with naturally acquired respiratory tract infections.

Comments/Critical Appraisal (including assessment of internal and external validity):

Evidence is provided by this study to support that early intervention with a standardized preparation of echinacea (Echinilin) was associated with a statistically significant decrease in the average severity and duration of common cold symptoms. One strength of this study compared to others looking at the use of echinacea for treatment of cold symptoms is that it actually investigated and analyzed the effect of echinacea on individual cold symptoms rather than grouping them all together for analyses. Specifically for sore throat, echinacea was shown to statistically significantly reduce the duration of this symptom by 0.7 of a day compared to placebo. No other trail that I have been able to find has done this. In terms of its internal validity, the strict inclusion and exclusion criteria of the study provides strength. However, the subjective nature of the patient scoring system and the uncertainty surrounding its validity weakens to internal validity of the study. Had the patient scoring system been utilized in combination with a validated clinician assessment and scoring system, this would have further strengthened the internal validity of the investigation. The external validity of this study is strengthened by the fact this was a

Canadian based study. However, the strict inclusion/exclusion criteria functions to weaken the external validity of the trial findings. Overall, considering this study assessed the efficacy of echinacea specifically on sore throat symptoms, the evidence it provides supports the use of echinacea for treating sore throat. However, further investigation is required to confirm or refute this evidence since few studies have focused on looking at the efficacy of echinacea specifically for the treatment of sore throat. In other words, this study was novel in the sense it looked at the effect of echinacea on specific common cold symptoms including sore throat and similar investigations are required to conform the evidence found.

3. Grimm W, Müller HH. A randomized controlled trial of the effect of fluid extract of Echinacea purpurea on the incidence and severity of colds and respiratory infections. Am J Med. 1999 Feb;106(2):138-43.

Extended Abstract:
Study Objectives: A randomized placebo-controlled double-blind study to determine the clinical efficacy of fluid extract of *Echinacea purpurea* on the incidence and severity of colds and respiratory infections.

Methods:
- Design: A randomized, double-blind, placebo-controlled trial.
- Allocation: A total of 108 patients with a history of more than 3 colds or respiratory infections in the preceding year were randomly assigned to receive 4 mL fluid extract of *E. purpurea* or 4 mL placebo-juice twice a day in a double-blind manner (54 patients were allocated to each treatment group). All study patients were assigned to an 8-week treatment period with either fluid extract of *E. purpurea* 4 mL twice daily or placebo juice 4 mL twice daily according to a computer-generated randomized list in a double-blind fashion.
- Blinding: Double-blind, randomized control trial.
- Follow-up Period: 8 weeks; Medical history, physical exam and hematologic examinations were performed at baseline, after 4 weeks and at the final visit 8 weeks after enrollment. Patients were also instructed to see the study investigator in the general practice at any time if he or she noticed any of the following signs and symptom; burning or tearing eyes, ear pain, loss of hearing with pressure in ear, stuffed nose, runny nose, sore throat, difficulty swallowing, hoarseness, coughing, sputum, headache, joint pain, myalgia, fever, rigors, sweating and general weakness or tiredness.
- Participants: A total of 109 patients with a history of more than 3 colds or respiratory infections in the preceding year were recruited for the study. One patient withdrew his consent prior to taking the first dose of allocated medication and thus, only 108 patients completed the study and were included for analysis. Patients were eligible for study inclusion if they reported more than 3 respiratory airway infections or common colds in the preceding year, were at least 12 years of age and had given written informed consent for study participation (parents gave written informed consent for those participants under the age of 18 years old). General exclusion criteria were acute infections of any kind within 1 week of recruitment, pregnancy or breastfeeding, use of immunostimulating drug within the 4 weeks before study entry, known allergy to coneflowers, severe underlying disease or immunosuppression, inability to give consent or unreliability for follow-ups as judged by investigators.
- Intervention: Fluid extract of *E. purpurea*(4 mL) compared to placebo-juice (4 mL), both taken twice daily. Investigators reported that the fluid extract and placebo were indistinguishable as to appearance, colour, flavour, packaging or labeling. Treatment duration was 8-weeks for both.

- Outcomes: The primary efficacy parameters were the incidence and severity of cold and respiratory infections during the 8-week treatment period according to a blinded investigator's assessment during regular or unscheduled patient visits. Presence and severity of colds and respiratory infections were determined by one of two general practice investigators based on patient symptoms together with findings on physical assessment.
- Patient Follow-up: The incidence and severity of colds and respiratory infections were determined during 8 weeks of follow-up, based on patient reported symptoms together with findings on physical exam. The severity of each infection was graded by the investigators. When a patient presented with symptoms and clinical findings that were considered by the investigator to result from a cold or respiratory infection, further follow-up visits were scheduled at 2- to 3-day intervals to determine duration and severity of the infection.
- Setting: Community, general outpatient practice in Dettelbach, Germany.

Main Results: No significant differences in the incidence, duration or severity of colds and respiratory infections were found in the *E. purpurea* or placebo-juice treatment groups. Both treatments were well tolerated by patients and the majority of adverse events were mild and transient and did not require discontinuation of treatment. Of the patients that dropped out of the echinacea group, reasons for withdrawal included nausea, constipation, palatability and patient choice without specific reason. Similar reasons were reported for patient withdrawing from the placebo group. Specifically looking at sore throat related conditions, 20 patients of the echinacea group and 28 patients from the placebo group were reported as experiencing pharyngitis. However, it is unknown whether this difference was statistically significant and statistics specifically looking at sore throat as a symptom were not analyzed by this study.

Conclusions: Prophylactic use and treatment of common cold or respiratory infections with fluid extract of *E. purpurea* did not decrease the incidence or severity of symptoms associated with these conditions compared to placebo. Further trials are required to evaluate the clinical efficacy of fluid extract of *E. purpurea*.

Comments/Critical Appraisal (including assessment of internal and external validity):

Selection of this article for critical appraisal was based on the fact that it has been cited in a variety of other review articles. Upon critically appraising it, the small sample size and failure to specifically analyze echinacea's potential for improving sore throat as a specific symptom in study participants were obvious limitations to its external validity. Furthermore, the fact that the *E. purpurea* fluid extract was used both prophylactically and as treatment for common cold or respiratory symptoms further limits this trials external validity as it relates to the topic of study which is the treatment of acute sore throat. In terms of internal validity, it is strong given the strict inclusion and exclusion criteria of the study. Its internal validity is further strengthened by the fact that both patient and clinical (investigator) assessments of patient symptoms were taken and analysis in a manner that was double-blinded. Overall, it is apparent from the discussions within the content of this paper that the clinical efficacy of fluid extract of *E. purpurea* for the prevention and treatment of cold symptoms, including sore throat, and respiratory infections is conflicting and further investigation is required.

4. Turner RB, Bauer R, Woelkart K, Hulsey TC, Gangemi JD. An evaluation of Echinacea angustifolia in experimental rhinovirus infections. N Engl J Med. 2005; 353(4): 341-8.

Extended Abstract:

Study Objectives: To systematically evaluate the efficacy of various carefully defined preparations of *Echinacea angustifolia* root extracts as a remedy (i.e. treatment) for rhinovirus infection and common cold symptoms.

Methods:

- Design: Randomized, double-blind, placebo controlled trial.
- Allocation: A total of 437 healthy volunteers were randomly assigned to receive either prophylaxis (beginning seven days before the virus challenge) or treatment (beginning at the time of the challenge) with one of three *E. angustifolia* root extracts (carbon dioxide, 60% ethanol, or 20% ethanol extracts) preparations or with placebo. Approximately 55 subjects were randomly allocated to each of the *E. angustifolia* root extract prophylactic- treatment groups, 55 subjects to each of the placebo prophylaxis-*E. angustifolia* root extract treatment groups and 109 subjects to the placebo prophylaxis-placebo treatment group. In summary, there were 6 cohort treatment groups totaling 328 subjects and 1 control group with a total of 109 subjects.
- Blinding: Double-blind, randomized, placebo controlled trial. All participants and study investigators were blinded to the group assignments.
- Follow-up Period: approximately 4 weeks.
- Participants: A total of 437 healthy volunteers susceptible to rhinovirus type 39, the virus frequently responsible for upper respiratory tract symptoms or the common cold, were recruited to participate in the study. Of the 437 initial volunteers, only 399 volunteers completed the study and were included in the data analysis. Reasons for this reduction in participants were due to voluntary withdrawal, illness and exclusion criteria. The mean (±SD) age of the 399 subjects was 20.8±3.3 years. Of these, 240 subjects (60 percent) were of female gender. The random assignment of subjects to the treatment groups resulted in a balanced distribution with regard to age, ethnicity and gender, with the exception of the treatment group that received the 60 percent extract, in which women were overrepresented (75 percent, P=0.02) as compared with the placebo group.
- Intervention: Study interventions consisted of three different *E. angustifolia* root extract (carbon dioxide, 60% ethanol, or 20% ethanol extracts) preparations and a placebo control. The treatments were given three times each day as a 1.5-ml tincture containing the equivalent of 300 mg of echinacea root. The study was divided into a prophylaxis phase (7 days prior to virus challenge) and a treatment phase (virus challenge until 5 days after). There were seven possible treatment assignments of *E. angustifolia*, with carbon dioxide extract, 60 percent extract, or 20 percent extract given during both phases or with placebo given during the prophylaxis phase and the carbon dioxide extract, 60 percent extract, or 20 percent extract of *E. angustifolia* given during the treatment phase. The control group received placebo throughout both phases of the study period. Volunteers took their assigned study medication as outpatients on starting 7 days prior to viral challenge. All asymptomatic volunteers were challenged with rhinovirus type 39 and then isolated in individual hotel rooms for the remainder of the study.
- Outcomes: The primary end point for the prophylaxis phase of the study (i.e., treatment with Echinacea 7 days prior to rhinovirus exposure through to study day 5 post-exposure) was the comparison of the proportion of volunteers who became infected with rhinovirus in each group with the proportion infected in the placebo group. The primary end point for the subjects given echinacea as treatment (i.e., those volunteers treated with Echinacea only from virus challenge to study day 5 post-exposure) was the comparison of the total symptom score for the infected subjects in each treatment group with the total symptom score for the infected subjects in the placebo group.

- Patient Follow-up: Starting in the morning 5 days after viral challenge, study participant symptom scores were evaluated every morning and evening, and a nasal lavage was performed each morning after symptom scoring was completed. Volunteers were asked to rate their symptoms of sneezing, rhinorrhea, nasal obstruction, sore throat, cough, headache, malaise, and chilliness on a scale of 0 to 4; the numbers corresponded to a symptom severity of absent, mild, moderate, severe, or very severe. The resulting symptom scores for each participant were recorded by study investigators. Scoring of symptoms was done before virus challenge and then every morning and evening on study days 1 to 5. Approximately three weeks after the virus challenge, all volunteers returned to the study site to have blood collected for testing for antibody to rhinovirus type 39. Compliance and blinding were also monitored and assessed through the study.
- Setting: Outpatient, community study, University of Virginia campus

Main Results: Prophylaxis with any of the echinacea preparations utilized within the study methods had no significant effect on rhinovirus infection and there was no effect on the infection rate in those groups that received echinacea only in the treatment phase of the study. The quantitative virus titer also was not affected by either prophylaxis or treatment with all the echinacea preparations. In terms of symptomatic relief, treatment with any of three *E. angustifolia* root extracts had no significant effect on symptoms associated with rhinovirus, whether assessed by the total symptom score or by the proportion of subjects with clinical colds. There was also no effect of either prophylaxis or treatment on the course of illness. In terms of side effects, gastrointestinal side effects were the most common side effects reported among the study participants.

Conclusions: Extracts of *E. angustifolia* root, either alone or in combination, do not have clinically significant effects on infection with a rhinovirus or on the clinical illness (i.e. common cold symptoms) that results from it.

Comments/Critical Appraisal (including assessment of internal and external validity):

The findings presented by this investigation further contribute to the conflicting evidence surrounding the use of echinacea for the treatment of common cold symptoms, specifically sore throat. One important thing to point out regarding this study is the fact that various preparations of *E. angustifolia* root extract were utilized. The body of conflicting evidence surrounding the use of echinacea for its immune stimulating properties and benefit for common cold symptoms, specifically sore throat, is derived from *Echinacea purpurea*. As such, the external validity of this study is largely limited by this and the fact that the availability of an *E. angustifolia* root extracts utilized with the trial is uncertain. Furthermore, given that the study failed to report the statistical analysis findings for each symptom individually, specifically sore throat, thus limits the study external validity making it harder to apply the study conclusions specifically to sore throat patients. Internal validity is also called into question by the combining of symptom scores for analysis as it raises the question of whether this was done to boost study power and statistically significant. However, the relatively large sample size of the study group and the fact this was a North American based trial function to strengthen its external validity. In terms of internal validity, it is strengthened by the fact that all patients were accounted for at follow up and all treatment groups were similar (balanced) in terms of patient-specific factors with the exception of one as noted in the extended abstract. Internal validity is further strengthened by the fact that it was a randomized, double-blind, placebo controlled trial which exposed patient to a viral infection commonly associated with causing common cold symptoms. Furthermore, the parameters and frequency of

monitoring performed as part of this study strengthens its internal validity as does the fact that study investigators assessed for and confirmed both blinding and compliance. Overall, after appraising the article, it was a well-designed clinical trial with relatively strong internal validity. Unfortunately, on the basis of the study conclusions drawn, it provides no evidence surrounding the use of echinacea for the treatment of sore throat.

Tertiary/Secondary:

5. Nahas R, Balla A. Complementary and alternative medicine for prevention and treatment of the common cold. Can Fam Physician. 2011; 57(1): 31-6.

Extended Abstract:

Study objectives: A systematic review of the evidence supporting complementary and alternative medicine approaches (including echinacea, garlic, ginseng, probiotics, vitamin C and zinc) to the treatment and prevention of the common cold in adults.

Scope - describe the scope of included studies (ex. patients, interventions, outcomes, duration, etc.)

Clinical trials and other prospective studies, systematic reviews and meta-analyses were included as part of this clinical review. Only trials evaluating single agents, mostly in healthy adults, were selected for inclusion. Specifically with regards to Echinacea, 11 trials were identified, 6 evaluated *Echinacea purpurea* in a total of 764 healthy adults with cold symptoms define by the investigators to include nasal congestion and discharge, sneezing, cough, sore throat and fever. These same 6 trails used 5 distinct preparations: 3 tinctures and 2 tablets derived from various extracts. Three of trials studied healthy adults while the other 3 studied adults with 2 or more colds in the previous year. Different clinical scoring systems were also used. Of the 4 trials that measured duration of symptoms, 3 found significant reductions ($P<0.05$ for all).

Methods – describe how studies were identified, number and type of trials included, and any other relevant information regarding the methods

Medline, Embase, and the Cochrane Database of Systematic reviews were searched from January 1966 to August 2009 using the key words common cold or influenza with echinacea, garlic, ginseng, probiotics, vitamin C and zinc. The interventions were selected based on literature reviews and clinical experience. Identified articles were then reviewed separately by study investigators.

Main results: Moderate evidence was found that *E. purpurea* might be effective for treatment of the common cold, but issues surrounding dose and formulation (according to the clinical review investigators) require clarification before it can be recommended for routine use. The typical dose reported for echinacea is 2000 to 3000 mg of crude extract, 6 to 9 mL of pressed juice, or 0.75 to 1.5 mL of tincture per day.

Conclusions: *Echinacea purpurea* might reduce duration and severity of cold symptoms when taken at the first signs of a cold. It is a safe option that might improve outcomes for patients with the common cold.

Comments/critical appraisal (including assessment of internal and external validity):

Unfortunately, similar to much of the evidence surrounding the use of *E. purpurea* for the treatment of cold symptoms, these is little focusing solely on whether *E. purpurea* directly improves sore throat symptoms. In other words, the review's failure to specifically investigate the potential of *E. purpurea* for improving sore throat as a specific symptom in study participants is an obvious limitation to its external validity. However, study investigators did defined a cold as including symptoms of nasal congestion and discharge, sneezing, cough, sore throat and fever. As such, although no study directly looking at improvement in sore throat symptoms with *E. purpurea* treatment was included as part of this literature review investigation, given *E. purpurea* was suggested to reduce the severity and duration of common cold symptoms (in general), one of which is sore throat, we can speculate that similar findings would exist has each individual symptom of the common cold been investigated. In other words, the evidence found supporting the use of *E. purpurea* for the treatment of common cold symptoms can be extrapolated to suggest it would also improve sore throat symptoms alone. However, evidence supporting this claim in scarce at best and further investigation would be required to confirm or refute this hypothesis. In terms of internal validity, it seems relatively strong overall. However, it is weakened by the fact that study investigators utilized clinical experience to select interventions for inclusion in the study. Doing so inserts potential bias into the research methods and weakens the inclusion/exclusion criteria of the review. The articles external validity is quite strong as the evidence obtain is widely applicable to the general population since the study population report in the review were healthy adults and the formulations utilized varied. Of note, as recognized by the study investigators, issues surrounding dose and formulation of *E. purpurea* require clarification before it can be recommended for routine use which weakens the external validity of the findings reported. Overall, this review article provides promising evidence that an extract of *E. purpurea* might be effective for the treatment of the common cold and thereby, sore throat symptoms.

6. **Natural Standard. Echinacea. http://www.naturalstandard.com.proxy.lib.uwaterloo.ca/databases. Accessed March 5, 2013.**

Source Description: Natural Standard is a database containing systematic review of scientific evidence on complementary and alternative medicine. Its editorial board contains MDs, NDs, PharmDs, PhDs, DC, Administrator of Ayurveda Institute, Director of the research group for Mind-Body dynamics at the Institute for Nonlinear Science and Ayurveda Physician, and Executive Director of Ayurvedic Institute of India. The database is generally updated every 3-18 months. However, it does not mention when each individual monograph was updated. Based on the evidence, the Natural Standard provides evidence grade and they are as follows: A – Strong positive scientific evidence, B – Positive scientific evidence , C – Unclear scientific evidence, D – Negative scientific evidence, F – Strong negative scientific evidence.

Summary: Natural standard cites a variety of conflicting evidence surrounding the use of various echinacea preparations and formulations for the treatment of the common cold and thereby sore throat. It states that oral preparations of echinacea are popular in Europe and the United States for the prevention and treatment of upper respiratory tract infections or the common cold of which sore throat is commonly a symptom. Echinacea is stated by Natural standard as possessing antimicrobial, antiviral and immunostimulatory effects all of which may be beneficial for the treatment of sore throat. Upon reviewing this literary source, it is quite evident there is a lack of specific evidence presented looking at the efficacy or use of echinacea alone or in combination therapy specifically for the treatment of sore throat. Much of the evidence cited in Natural Standard surrounding the use of echinacea is for treatment of the common cold, specifically upper respiratory tract infections. Natural Standard defines the common cold as including sore throat as a symptom and thus, the reviewer is left to extrapolate

evidence of benefit for treatment of sore throat from that found for treatment of the common cold. In other words, Natural Standard does not provide any explicit evidence that echinacea would be beneficial or efficacious in the treatment of sore throat alone but conclusions can be drawn from the trails supporting the use of echinacea for treatment of the common cold. Much of the evidence cited in Natural Standard surrounding the use of echinacea for common cold symptoms is derived from Goel et al. and Turner et al. which both were looking at sore throat as one of many symptoms associated with the common cold rather than sore throat as a symptom on its own.

Overall, echinacea is rated as evidence grade B for the treatment of upper respiratory tract infections in adults by Natural Standard but no specific evidence grade is given for sore throat. In terms of side effects, Echinacea is stated as being well tolerated with gastrointestinal upset and rash occurring most frequently.

Comments/critical Appraisal: The information provided on Natural Standard is internally valid since it considered primary literature to support a recommendation of grade B for the use of echinacea in the treatment of upper respiratory tract infection symptoms. Natural standard clearly defines its grading criteria for recommendations based on quality of evidence. Unfortunately, Natural standard does not explicitly provide evidence surrounding the use of echinacea for the treatment of sore throat. Readers are left to extrapolate such evidence from the effect of echinacea in reducing common cold symptoms, one of which is sore throat. As such, despite its strong internal validity, the external validity for the use of echinacea in the treatment of sore throat is largely limited since there is not a large body of evidence directly supporting this use.