Clinical Studies on Echinacea (*Echinacea* spp.)

Cold/Flu/Upper Respiratory Tract Infection (URTI) Treatment

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Brinkeborn *et al*., 1999	URTI symptoms	R, DB, PC (4 arm) n=246 subjects with colds	7 days from the start of acute URTI (1–2 days of symptoms)	2 tablets, 3x/day	Echinaforce® concentrate, special *E. purpurea* root preparation	Relative reduction in complaint index for 12 symptoms in the 4 groups differed significantly (p=0.015). Echinacea patients reductions in complaint index were significantly higher than in the placebo group (p=0.003 and p=0.020). Echinacea was concluded to be a low-risk, effective alternative for symptomatic acute treatment of the common cold.
Brinkeborn *et al*., 1998	URTI symptoms	R, DB, PC n=119	8 days from the start of acute URTI (1–2 days of symptoms)	Two, 400 mg tablets 3x/day	Echinaforce® tablet	Based on 12 symptoms, the "overall clinical picture" for the intention-to-treat was reduced in the treatment group from 9.0 to 4.1 (p=0.045), while the placebo group decreased from 8.8 to 5.3. Echinacea was concluded to be a low-risk, effective alternative for symptomatic acute treatment of the common cold.
Dorn *et al*., 1997	URTI symptoms	R, DB, PC n=160 (ages >18 years)	8–10 days from onset of flu-like respiratory symptoms	45 drops extract 2x/day (equivalent to 900 mg/day)	Brand not stated	The length of the illness decreased from 13 to 9.8 days (bacterial infections) and to 9.1 days (viral infections) compared to placebo (p=0.0001). The infection type was determined by lymphocyte and neutrophil counts in the blood. Echinacea appears to shorten the duration of URTIs.
Hoheisel *et al*., 1997	URTI symptoms	R, DB, PC n=120 with at least 3 infections in the past 6 months	10 days from the first sign of URTI, before full development	20 drops, every 2 hours on day 1, 20 drops, 3x/day thereafter	Echinaguard® extract	Of the echinacea group, 40% developed a "real cold" compared to 60% in the placebo group (p=0.044), while in 4 days symptoms improved for echinacea group compared to 8 days for the placebo group. Echinacea showed more rapid recovery in the intention-to-treat population (p<0.0001).
Galea and Thacker, 1996	URTI symptoms	R, DB, PC, P n=190	From the first sign of URTI through 10 days	250 mg capsule	*E. angustifolia* root dried (brand not stated)	8 symptoms were assessed and no measurable benefits were reported, attributed to the relatively low dose and lack of severity of the symptoms being measured.
Bräunig *et al*., 1992	Flu-like symptoms	R, DB, PC n=180 one group of 60 per preparation	From onset of flu-like respiratory symptoms until symptoms subsided	90 drops (450 mg)/day or 180 drops (900 mg)/day	*E. purpurea* root extract (1:5, 55% ethanol) (brand not stated)	Echinacea patients receiving 180 drops (900 mg) dose displayed statistically significant improvement (p<0.05) compared with placebo group in relieving symptoms and decreasing the duration of symptoms. The study suggests that dosage influences effectiveness.

Combination Preparations (Treatment)

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Lindenmuth and Lindenmuth, 2000	Cold, flu-like, URTI symptoms	R, DB, PC n=95 with early symptoms of cold or flu, primarily females (mean age 39.7 years)	From first sign of flu-like symptoms through 6 days	5–6 cups tea first day of symptoms and titrating down 1 cup of tea/day for next 5 days (equivalent of 1,275 mg dried herb and root per tea bag serving)	Echinacea Plus® tea vs. Traditional Medicinals Eater's Digest® herbal tea (placebo)	Based on questionnaire on effectiveness of echinacea, duration of symptoms, and time taken for subjects to notice any changes in symptoms, echinacea group was shown to be statistically significant in effectiveness (p<0.001); duration (p<0.001); and in noticeable change in symptoms (p<0.001). Authors concluded that treatment with echinacea compound tea, given at early onset of symptoms was effective in relieving cold or flu symptoms in noticeably fewer days compared to placebo.
Henneicke-von Zepelin *et al*., 1999	Common cold (acute viral URTI)	R, DB, PC, MC (15 centers) n=238 patients (ages 18–70 years)	7–9 days once identified as having a common cold	3 tablets 3x/day	Esberitox® N2 tablet vs. placebo	The echinacea combination product was significantly better than placebo (p=0.0497), with highly statistically significant results in overall well-being (p=0.0048), rhinitis, and bronchitis scores. This study suggests this is a safe and effective treatment and notes the greatest benefits would be experienced if treatment is started as soon as possible after onset of the cold.

KEY: C – controlled, **CC** – case-control, **CH** – cohort, **CI** – confidence interval, **Cm** – comparison, **CO** – crossover, **CS** – cross-sectional, **DB** – double-blind, **E** – epidemiological, **LC** – longitudinal cohort, **MA** – meta-analysis, **MC** – multi-center, **n** – number of patients, **O** – open, **OB** – observational, **OL** – open label, **OR** – odds ratio, **P** – prospective, **PB** – patient-blind, **PC** – placebo-controlled, **PG** – parallel group, **PS** – pilot study, **R** – randomized, **RC** – reference-controlled, **RCS** – retrospective cross-sectional, **RS** - retrospective, **S** – surveillance, **SB** – single-blind, **SC** – single-center, **U** – uncontrolled, **UP** – unpublished, **VC** – vehicle-controlled.

Clinical Studies on Echinacea (*Echinacea* spp.) (cont.)

Combination Preparations (Treatment) (cont.)

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Reitz,1990	URTI symptoms and signs	R, DB, PC n=150	8 weeks initially, with monitoring for an additional year	One, 22.5 mg tablet 3x/day or placebo (vitamin C)	Esberitox® N1 tablet vs. placebo	Majority of symptoms and signs at 7 and 14 days were significantly better than placebo; nasal symptoms were most affected. No difference in result from blood work was reported.
Dorn, 1989	URTI symptoms and signs	R, DB, PC n=100	From 2 days of URTI onset	Day 1–2: 30 ml/day Day 3–6: 15 ml/day	Resistan® vs. placebo	Echinacea patients experienced a decrease in the length of illness and severity in 7 of 7 self-assessed symptoms compared to 4 of 7 in placebo group (p=0.001). The study suggests that taking the preparation as soon as symptoms first appear shortens duration of URTI.
Vorberg and Schneider, 1989	URTI symptoms and signs	R, DB, PC n=100	10 days beginning 2 days after onset of URTI	15–30 ml/day	Resistan® vs. placebo	Most symptoms were significantly better in the echinacea group compared to placebo at both 2 to 3 days and at 8 to 10 days. The results indicate echinacea has efficacy for the prevention and treatment of URTIs.
Vorberg, 1984	URTI symptoms and signs in patients suffering from common cold	R, DB, PC n=100	10 days	15 mg tablet 3x/day	Esberitox® tablet vs. placebo	Echinacea group reported significant superiority compared to placebo group in all examined parameters of common cold (p<0.001) including fatigue, reduced performance, runny nose, and sore throat.

Cold/Flu/URTI Prevention

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Grimm and Müller, 1999	URTI occurrence	R, PC n=108 with history of 3 colds or respiratory infections in the preceding year (mean age echinacea group 42 years; mean age placebo group 38 years)	2 months	4 ml expressed juice 2x/day	*E. purpurea* fluid (expressed juice of aerial parts, brand not stated, though test material was provided by Madaus AG and it presumably is Echinacin®)	During 8-week treatment period, 35 (65%) of 54 patients in echinacea group and 40 (74%) of 54 patients in placebo group had at least one cold or respiratory infection (relative risk [RR]=0.88; 95% confidence interval [CI] [0.60, 1.22]). Average number of colds and respiratory infections per patient was 0.78 in echinacea group, and 0.93 in placebo group (difference=0.15; 95% CI [-0.12, 0.41], p=0.33). Median duration of colds and respiratory infections was 4.5 days in echinacea group and 6.5 days in placebo group (95% CI [-1, +3 days]; p=0.45). There were no significant differences between treatment groups in number of, duration, or severity of colds. Side effects were observed in 11 patients (20%) of echinacea group and in 7 patients (13%) of placebo group (p=0.44).
Melchart *et al*., 1998	URTI occurrence	R, DB, PC n=289 (ages 18–65 years)	12 weeks (M-F only)	50 drops *E. angustifolia* 2x/day or 50 drops *E. purpurea* 2x/day or placebo	*E. angustifolia* and *E. purpurea* roots extracts (1:11 in 30% ethanol) (brand not stated)	Participants in treatment group believed they had more benefit than placebo group (p=0.04). URTIs (at least one) were experienced by 32%, 29%, and 37% of *E. angustifolia*, *E. purpurea*, and placebo groups respectively, and onset was at 66, 69, and 65 days, respectively, with no significant differences in duration, incidence, or severity of URTIs. Noncontinuous administration of treatment was not addressed in the conclusion.
Schöneberger, 1992	URTI occurrence	R, DB, PC, MC n=108 patients with increased susceptibility to colds (suffered at least 3 colds in previous year) (ages 13–84 years)	2 months	4 ml 2x/day	Echinacin®	Echinacea group experienced decreased in URTI incidence in 35% (vs. 26%), decrease in duration of 5.34 days (vs. 7.54 days), increase in interval between infections of 40 days (vs. 25 days), and decreased severity of symptoms calculated as 78% (vs. 68%) compared with placebo. Patients with weakened defense (calculated as a T4/T8-ratio of less than 1.5) benefited most.

KEY: C – controlled, **CC** – case-control, **CH** – cohort, **CI** – confidence interval, **Cm** – comparison, **CO** – crossover, **CS** – cross-sectional, **DB** – double-blind, **E** – epidemiological, **LC** – longitudinal cohort, **MA** – meta-analysis, **MC** – multi-center, **n** – number of patients, **O** – open, **OB** – observational, **OL** – open label, **OR** – odds ratio, **P** – prospective, **PB** – patient-blind, **PC** – placebo-controlled, **PG** – parallel group, **PS** – pilot study, **R** – randomized, **RC** – reference-controlled, **RCS** – retrospective cross-sectional, **RS** - retrospective, **S** – surveillance, **SB** – single-blind, **SC** – single-center, **U** – uncontrolled, **UP** – unpublished, **VC** – vehicle-controlled.

Clinical Studies on Echinacea (*Echinacea* spp.) (cont.)

Combination Preparations (Prevention)

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Schmidt *et al.*, 1990	URTI occurrence	R, DB, PC n=609 college students	2 months	12 ml/day	Resistan® vs. placebo	Echinacea patients experienced 15% fewer primary infections, and relapses decreased by 27%, or relative risk reduction of 12%. Due to potential immuno-stimulant activity of other botanicals, the results could not be attributed to echinacea alone.
Forth and Beuscher, 1981	URTI occurrence	R, PC (not fully double-blind) n=95	16 weeks (November through February)	25 drops 3x/day or 1 mg tablet or placebo	Esberitox®	Patients had relative risk reduction of 49% overall, even though no apparent difference for other 7 symptoms was observed in all groups compared to placebo. However, improvement of nasal symptoms was significant.

Other

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Vonau *et al.*, 2001	Effect on clinical course of genital herpes	SC, P, DB, PC, CO n=50 (mean age 36.5 years)	1 year (6 months placebo, 6 months echinacea)	800 mg 2x/day	Echinaforce® tablet	No statistically significant benefit was shown for use of echinacea to treat frequently recurring genital herpes.
Gallo *et al.*, 2000	Safety of gestational exposure to echinacea	P, C n=206 patients who used echinacea during pregnancy	Until birth or termination of the pregnancy n=112 (echinacea used during first trimester)	Range of 250–1,000 mg/day capsule or tablets taken by 114 females or range of 5–10 to 30 drops maximum/day taken by 76 females continuously for 5–7 days	Primarily *E. angustifolia* and *E. purpurea*; only one reported using *E. pallida* (brand not stated)	Of 206 subjects who used echinacea during pregnancy, there were 195 live births, 13 spontaneous abortions, and one therapeutic abortion, compared to the control group giving 198 live births, 7 spontaneous abortions, and 1 therapeutic abortion. These results indicated no statistical differences between the 2 groups in terms of pregnancy outcome, delivery method, maternal weight gain, gestational age, birth weight, or fetal distress. Rates of major malformation between study and control groups were not statistically different.
Berg *et al.*, 1998	Exercise-induced immunological effects	R, PC, PG n=42 male athletes, 3 groups (mean age 27.5 years)	28 days (prior to triathlon)	40 drops 3x/day (8 ml/day) (n=14) or magnesium (n=13) or placebo (n=13)	Echinacin®	Echinacea facilitated IL-6 release and reduced SIL-2R release in serum and urine, significantly increased serum cortisol (one hour after the event), and may exert slight effects on natural killer cells and T-cells. Echinacea group did not report any URTIs compared to 7 total from 2 other groups, along with 6 reporting other infections.
Coeugniet and Kuhnast, 1986	Chronic candidiasis in females	OL, Cm (5-arm) n=203	10 weeks	30 drops 3x/day with cream for 6 days (n=60) or cream alone (6 days only) (n=43)	Echinacin® and econazole nitrate cream (antimycotic treatment)	Use of echinacea as adjunct therapy reduced recurrence rate 5–16% compared to women using only cream, who experienced a recurrence rate of 60.5%.

KEY: **C** – controlled, **CC** – case-control, **CH** – cohort, **CI** – confidence interval, **Cm** – comparison, **CO** – crossover, **CS** – cross-sectional, **DB** – double-blind, **E** – epidemiological, **LC** – longitudinal cohort, **MA** – meta-analysis, **MC** – multi-center, **n** – number of patients, **O** – open, **OB** – observational, **OL** – open label, **OR** – odds ratio, **P** – prospective, **PB** – patient-blind, **PC** – placebo-controlled, **PG** – parallel group, **PS** – pilot study, **R** – randomized, **RC** – reference-controlled, **RCS** – retrospective cross-sectional, **RS** - retrospective, **S** – surveillance, **SB** – single-blind, **SC** – single-center, **U** – uncontrolled, **UP** – unpublished, **VC** – vehicle-controlled.