

# The Efficacy of Echinacea Compound Herbal Tea Preparation on the Severity and Duration of Upper Respiratory and Flu Symptoms: A Randomized, Double-Blind Placebo-Controlled Study

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## ABSTRACT

**Objectives:** The aim of this study was to determine the efficacy of an echinacea compound herbal tea preparation (Echinacea Plus<sup>®</sup>) given at early onset of cold or flu symptoms in a random assignment double-blind placebo-controlled study.

**Design and Subjects:** A total of 95 subjects with early symptoms of cold or flu (runny nose, scratchy throat, fever) were randomly assigned to receive Echinacea Plus tea five to six cups per day titrating to 1 over 5 days or placebo in a double-blind situation. Each participant completed a questionnaire 14 days after beginning the program. The efficacy, number of days the symptoms lasted, and number of days for change were measured with a self scoring questionnaire.

**Results:** The study period was 90 days (January 1, 1999 to March 30, 1999). There was a significant difference between the experimental group (Echinacea Plus) and control group (placebo) for all 3 questions measured:  $p < 0.001$ . There were no negative effects reported by any of the subjects in either group.

**Conclusions:** Treatment with Echinacea Plus<sup>®</sup> tea at early onset of cold or flu symptoms was effective for relieving these symptoms in a shorter period of time than a placebo.

## INTRODUCTION

In recent years the American public has become enamored with herbal remedies, yet there has been a scarcity of scientific research. Echinacea preparations have become the best-selling herbal immunostimulants in Europe and North America with most products being manufactured from the aerial parts and/or root of *Echinacea purpurea* (L.) Moench (Asteraceae) or from the roots of *E. angustifolia* DC and *E. pallida* (Nutt.) Nutt. Of the more than 800 echinacea-containing drugs on the market in Germany today, most products are composed of

either the expressed juice of the aerial parts of *E. purpurea* or they are hydroalcoholic tinctures of the roots of *E. pallida* and/or *E. purpurea* (Bauer, 1998, 1999b). The roots and the aerial parts of *E. purpurea* are used for comparable medicinal purposes as *E. angustifolia* and *E. pallida* (Bauer, 1999b). The Genus *Echinacea* includes nine species found in the United States and Canada (McGregor, 1968). The territories of the native Americans who used Echinacea medicinally closely corresponds to the natural distribution range of the three primary species *E. angustifolia*, *E. pallida*, and *E. purpurea*, although it is possible that other species were

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also used (Bauer, 1998; Flannery, 1999). Native Americans used various Echinacea preparations to treat such problems as wounds, snake bites, tonsillitis, headache, and the cold symptoms (Hobbs, 1989). For example, the Choctaw people of Louisiana used *E. purpurea* root as a cough medicine (Flannery, 1999; Moerman, 1998) and the Comanche people used it to treat sore throats (Flannery, 1999). The Cheyenne people of Oklahoma and Montana prepared an aqueous infusion of the leaf and root of *E. angustifolia* for treatment of sore throat. The Cheyenne also prepared an infusion of *E. angustifolia* leaf for treatment of toothache (Moerman, 1998). *E. purpurea* was the first Echinacea species reported by nineteenth century American physicians and medical botanists for its therapeutic properties (Flannery, 1999). However, by the twentieth century American eclectic physicians had developed a preference for the *E. angustifolia* species, the 1852 edition of the Eclectic Dispensatory of the United States listed *E. purpurea* under the common name "red sunflower" (Flannery, 1999; King and Newton, 1852). Echinacea preparations were introduced into homeopathic medicine during the 1920s (Flannery, 1999). The therapeutic use of *E. purpurea* herb (leaf and flower) was introduced into Germany in the early part of the twentieth century by Gerhard Madaus (Bauer, 1999b; Madaus, 1939). Dr. Madaus cultivated *E. purpurea* in Germany and as a result most European research since the 1930s has been conducted on the *E. purpurea* species (Flannery, 1999). The fresh flowering aerial parts of *E. purpurea* are official in the *German Homeopathic Pharmacopoeia (GHP)* as is the fresh flowering plant, with roots, of *E. angustifolia* (GHP, 1989). The whole flowering plants of *E. angustifolia* and *E. purpurea*, respectively, are also official drugs of the *Homeopathic Pharmacopoeia of the United States* (1992) in the hydroalcoholic tincture form. In 1999, the World Health Organization published a therapeutic monograph for the fresh or dried aerial parts of *E. purpurea* harvested in full bloom (WHO, 1999). And in 2000, the European Scientific Cooperative on Phytotherapy is publishing its therapeutic monograph for the aerial parts of *E. purpurea* in the crude or processed state in appropriate dosage units (ESCO, 2000). Additionally, aqueous in-

fusions and/or decoctions prepared from the dried root of *E. purpurea* are regulated as Traditional Herbal Medicines (THM) in Canada and are indicated for the relief of sore throat due to colds (Health Canada, 1999).

Although various species of Echinacea have shown an effect, *E. purpurea* has been the species used most often for treatment of cold, flu, and upper respiratory illnesses (Melchart et al., 1995; Burger et al., 1997). Although all three of the abovementioned species have a long history of medical use in Europe and North America, most scientific studies have been conducted on preparations composed of the aerial parts of *E. purpurea* and, to a lesser extent, *E. angustifolia* (Foster, 1991, 1999). Systematic fractionation and pharmacologic testing of the aqueous extracts of the aerial parts of the *E. purpurea* lead to the isolation of two polysaccharides with immunostimulating properties (Wagner and Proksch, 1981). They were shown to stimulate phagocytosis *in vitro* and *in vivo*, and to enhance the production of oxygen radicals by macrophages in a dose-dependent manner (Stimpel et al., 1984). There continue to be problems with analyses of these components as the methods are in continuing development (Bauer, 1998). The analysis of polysaccharides in Echinacea is possible by specific determination only by isolation and structure elucidation or by nonspecific determination by hydrolysis of monosaccharides; neither of these methods are commercially available at this time (Bauer, 1999a). *E. angustifolia* (another component of Echinacea Plus [Traditional Medicinals<sup>®</sup>, Inc., Sebastopol, CA]) has also been shown in combination with other types of Echinacea to have a positive effect on immune system response concerning cold and flu symptoms (Melchart et al., 1995).

Clinical studies have looked at various intervals for the use of Echinacea in the prevention and treatment of cold and flu symptoms. For example there have been some differences in research findings on the efficacy of Echinacea as a prophylactic or long term preventative. One study relates that in a 6-month double-blind placebo study, the group given expressed juice of the aerial parts of *E. purpurea* had a lower frequency of respiratory reinfections (32% versus 19%), an increase in length

of interval between 25 versus 40 days), a reduction in the average duration of colds (7.5 versus 5.3 days), and less severe symptoms (Schöneberger, 1992). In a recent study, however, reported in the *American Journal of Medicine*, Grimm and Müller (1999) reported that the expressed juice of the aerial parts of *E. purpurea* given prophylactically over a 3-month period did not significantly decrease the incidence, duration, or severity of colds compared to a placebo. Further, there is some speculation to suggest that alcoholic extract of *E. purpurea* root reduces the strength of the immune system response when used continuously for long periods of time (Jurcic et al., 1989).

Much of the recent research focuses on relieving the symptoms and duration of colds and flu like infections by early intervention with Echinacea. For example Bräunig et al. (1992) demonstrated a statistically significant improvement of symptoms over placebo with early intervention with alcoholic tincture of *E. purpurea* roots, (1:5 (w/v), ethanol 55% V/V). Hoheisel, Sandberg et al. (1997), in a randomized, double-blind, single-center placebo-controlled study demonstrated that the use of an expressed juice of the aerial parts of *E. purpurea* given from the first signs of an upper respiratory infection or cold, both inhibits the full expression of the infection and speeds the recovery time. A meta-analysis of 26 controlled clinical trials (18 randomized, 11 double blind) on the immunomodulatory effects of echinacea was conducted by Melchart et al. (1994); of the 18 randomized trials, 16 claimed positive results, suggesting that preparations containing extracts of echinacea can be clinically effective immunomodulators. Further review of trials by Melchart and associates (1998) has indicated that there are some Echinacea compounds that may be better than a placebo. Although the majority of research studies showed positive results, there is not at this time sufficient evidence to support a specific Echinacea product.

There has been much further controversy over the efficacy of tablet versus liquid extract. The digestibility and absorption of the pill forms of Echinacea have been reviewed and debated in numerous articles. Most researchers agree that the liquid forms, either in an alcohol base or tea, are best for maximum absorption

(Wichtl and Bisset, 1994; British Herbal Medicine Association, 1996).

The objectives of this research are to test the efficacy of Echinacea compound herbal tea preparation on duration and severity of symptoms of scratchy throat, runny nose, and fever using a randomized double-blind study.

## METHODS

### *Sample*

Subjects of this study were employees of Rest Haven-York, an 167-bed nursing and rehabilitation center in York, Pennsylvania, located in south central Pennsylvania. Employees were eligible for the study if they reported the earliest symptoms of cold or flu: runny nose, scratchy throat, fever, etc. Subjects who were excluded included pregnant or breast-feeding mothers, persons who had known allergies to coneflowers or those who claimed to be allergic to many different flowering plants and pollens, and those who had acute infections and were already taking antibiotics.

### *Assignment*

All employees were first informed of the study in December 1998 and given information sheets on Echinacea. They were further informed that beginning January 1, 1999 through March 30, 1999, at the earliest sign of cold or flu symptoms (runny nose, scratchy throat, fever), they could volunteer to report for assignment to an experimental or control group for testing the effectiveness of Echinacea. Subjects were randomly assigned throughout this period to either the experimental group (echinacea) or control group (placebo). The random assignment was accomplished by specific trained secretarial personnel not associated with this study and having no prior knowledge of the groups or of which of the two boxes of tea bags contained the packets of Echinacea Plus tea bags and that contained the packets of placebo tea bags. These personnel used a numbered system for notating subjects' names and from which box each subject received a packet of tea bags. Due to not knowing how many employees would ultimately present themselves

for treatment, allocation was accomplished by utilization of alternation for assignment in order to keep the groups balanced. On reporting to this secretarial personnel, each subject was given a packet containing 21 tea bags of same appearance (wrapping) of either Echinacea Plus or placebo. The researchers were not involved in this process and did not know which set of tea bags (treatment or placebo) any participant received.

Echinacea Plus, an herbal dietary supplement, contains a proprietary blend of the leaves, flowers, and stems of organically grown *E. purpurea* and *E. angustifolia* plus a water soluble dry extract of *E. purpurea* root (6:1). In combination, this delivers the equivalent of 1,275 mg of dried herb and root per tea bag serving. (Certificates of authenticity are available on request.) When prepared according to label directions, a minimum 31.5 mg of total phenolic compounds (calculated as caftaric acid, cichoric acid, chlorogenic acid, and echinacoside) are yielded in one dose of brewed tea, as determined by high-performance liquid chromatography (HPLC). The herbal mixture additionally contains small amounts of two adjuvant components, lemongrass leaf (*Cymbopogon citratus* [DC. ex Nees] Stapf.) and spearmint leaf (*Mentha spicata* L.). At higher dosage these components might have an effect; however, both lemongrass leaf and spearmint leaf occur in the formula as "flavor corrigents" that are allowed in an herbal tea formula at up to 20% of the formula to make it reasonably palatable in order to assure patient compliance and tolerance; mint leaf is a widely used flavor corrective in medicinal herbal preparations (Schilcher, 1997; Weiss, 1998). The aerial parts of *E. angustifolia* DC. and *E. purpurea* (L.) Moench. (Asteraceae) contained in this product were grown at Trout Lake Farm Co., in Trout Lake, Washington, and corresponding voucher specimens are deposited at R.L. McGregor Herbarium, University of Kansas, Lawrence, Kansas. The echinacea root dry extract ingredient contained in this product was manufactured by Emil Flachsman AG, of Zurich, Switzerland (Product No. 85.030 Extr. Echinaceae purp. e. rad. spir. sicc.), which passed botanical identity tests based on chemistry composition including HPLC test for alkalamides, photometric test for phenolic com-

pounds, and an HPLC test for olig.  $\beta$ -1,2-fructofuranosides. According to an independent HPLC determination of phenolic compounds in the prepared infusion carried out by Industrial Laboratories of Denver, Colorado, the following results were obtained: 2 caffeoyl tartaric acid = 10.463 mg; cichoric acid = 16.977 mg; chlorogenic acid = ND; echinacoside = 4.055 mg with total phenolic compounds = 31.495 mg. (Analyses available upon request.) Specific instructions for boiling, steeping and dosage were given to each subject as follows: Pour 8 ounces of boiling water over one tea bag and steep, covered, for 10–15 minutes. Drink 5–6 cups on the first day of symptoms titrating to 1 cup by the fifth day.

#### *Placebo (control)*

Eater's Digest<sup>®</sup> (Traditional Medicines<sup>®</sup> Inc., Sebastopol, California) herbal tea was selected for the control tea because the formula basically promotes healthy digestion and would not be expected to improve or worsen common cold or flu symptoms. At higher dosage the cinnamon, ginger, and peppermint might have an effect, but in the included amounts serve the purpose of flavor correctives (Schilcher, 1997; Weiss, 1998). Furthermore, this tea does not contain any stimulants such as caffeine and does not have any obvious or easily recognizable aroma or flavor characteristics that would make it easily distinguishable from the Echinacea Plus tea by an untrained palate. It is unlikely that study volunteers would have seasoned herbal tea palates familiar with the characteristic taste of echinacea compound, particularly in the context of a multiherb formula containing some mint leaf. It should be noted that both the drug and placebo teas in this study contained mint leaf. The possibility would have been to add a natural flavor component to both teas in an effort to mask any known characteristic flavors, but the problems with that approach are twofold. Flavored teas are generally not perceived to be medicinal, which could have influenced the outcome because volunteers may have needed to believe that they were drinking a medicinal herbal tea. A second problem is that, by adding any new ingredient such as natural flavor to the for-

mula, the composition of the drug being studied is no longer exactly the same as the drug in commerce (Echinacea Plus). Additionally, each single dose of experimental tea and control tea was individually wrapped and sealed in a plain white, unprinted, tamper-evident, heat-sealed overwrap composed of paper with a 12-pound PVDC coating and 15-pound polyethylene surlin liner. The moisture vapor-transmission and oxygen-transmission properties of the overwrap film material provide an effective barrier preventing olfactory or visual differentiation by the subjects. The control tea contained Peppermint leaf (*Mentha x piperita* Linne), Sweet Fennel seed (*Foeniculum vulgare* Miller ssp. *vulgare*, var. *dulce* (Miller) Thellung), Ginger rhizome (*Zingiber officinale* Roscoe), Rose hip (*Rosa canina* L.), Papaya leaf (*Carica papaya* L.), Alfalfa leaf (*Medicago sativa* L.), and Cinnamon bark (*Cinnamomum cassia* J. Presl.). (Certificates of authenticity are available on request.) The same specific instructions for boiling, steeping, and dosage were given to each subject in this group as in the treatment group.

#### Dosage

Bräunig and Knick (1993) reported that a daily dose of 90 drops of a hydroalcoholic tincture (1:5), with a phytoequivalency of 900 mg dried echinacea roots, can be effective in reducing symptoms as compared to 450 mg in a placebo group. Traditional Medicinals, Inc. recommends ingesting 3–5 cups per day of the echinacea formula, containing 1000 mg or more echinacea per cup of tea. The protocol for this study was established at 5 to 6 cups the first day of symptoms and titrating down 1 per day for the next 5 days. The control (placebo) group was also placed on this protocol. The teas were bagged for the experimental and control groups in plain white wrappers to avoid identification by subjects.

#### Questionnaire

A simple three-question questionnaire was designed and given to subjects 14 days after they started the program. Question 1 looked at the effectiveness of the tea at relieving cold or flu symptoms. Question 2 looked at the num-

ber of days cold and flu symptoms lasted and question 3 looked at how long it took for the subjects to notice a difference in their symptoms. (See Table 1 for questionnaire and Table 2 for scoring code).

#### Hypotheses

1. There is a significant difference in effectiveness of relieving cold or flu symptoms between the experimental group (echinacea) and control group (placebo).
2. There is a significant difference between the experimental group (echinacea) and control group (placebo) in the number of days the symptoms lasted.
3. There is a significant difference between the experimental group (echinacea) and control group (placebo) in the number of days it takes to notice a difference.

#### Null hypotheses

Questions:

1. Experimental group = control group
2. Experimental group = control group
3. Experimental group = control group

#### Statistical analysis

Each question was analyzed separately using a mean, standard deviation, and *t* test. Confidence intervals of 95% were utilized with statistical significance set at  $p < 0.05$  level (two-tailed).

## RESULTS

A total of 95 subjects participated in the study (48 in the experimental group, 47 in the control group). Both groups consisted primarily of women (41 in the experimental group, 40 in the control group). This imbalance was due to the employment percentage for this facility (nursing home), which is 93% female. The age range for the subjects was from 24 to 62 with a mean age of 39.7, a median age of 40, and a mode of 28. Subjects included registered nurses, licensed practical nurses, maintenance personnel, dietary staff, therapists, administrators, accountants, and physicians. Rest Haven-

TABLE 1. ECHINACEA STUDY QUESTIONNAIRE

1. Please rate on the following scale the effectiveness of the tea at relieving your cold and/or flu symptoms:					
1 (Not effective)	2 (Fair)	3 (Medium)	4 (Good)	5 (Excellent)	
2. Please circle the number of days your cold and flu symptoms lasted:					
Less than 5	6	7	8	More than 10	
3. Please circle the number of days it took before you began to notice a difference in your symptoms:					
Immediately	2	3	4	More than 5	Not at All

York is located close to an inner city area and borders a suburban area. Sixty percent (60%) of the participants live in suburban and rural areas and 40% live in the inner city. All subjects who volunteered for the study remained in the study and completed the tea regimen and the questionnaire, and were included in the analyses. All subjects reported that they followed the exact dosage specifications.

#### Question 1

There was a significant difference between the experimental group (echinacea) versus the control group (placebo) in effectiveness of symptom relief. Experimental group, mean = 4.125, SD = 0.9593; control group, mean = 2.787, SD = 0.9541;  $t = 6.814$ ;  $p < 0.001$ .

#### Question 2

There was a significant difference between the experimental group (echinacea) versus the control group (placebo) in number of days of symptoms. Experimental group, mean = 4.333, SD = 0.9302; control group, mean = 2.340, SD = 1.088;  $t = 9.499$ ;  $p < 0.001$ .

#### Question 3

There was a significant difference between the experimental group (echinacea) versus the control group (placebo) in days of noticeable symptom change. Experimental group, mean = 3.854, SD = 0.9735; control group, mean = 2.297, SD = 1.204;  $t = 6.865$ ;  $p < 0.001$ .

Consequently the null hypotheses may be rejected.

TABLE 2. ECHINACEA STUDY QUESTIONNAIRE: CODING

1. Please rate on the following scale the effectiveness of the tea at relieving your cold and/or flu symptoms:					
1 (Not effective) (1)	2 (Fair) (2)	3 (Medium) (3)	4 (Good) (4)	5 (Excellent) (5)	
2. Please circle the number of days your cold and flu symptoms lasted:					
Less than 5 (5)	6 (4)	7 (3)	8 (2)	More than 10 (1)	
3. Please circle the number of days it took before you began to notice a difference in your symptoms:					
Immediately (5)	2 (4)	3 (3)	4 (2)	More than 5 (1)	Not at All (0)

Numbers in parenthesis show numerical coding for statistical analysis. The coding was arranged in a way to prevent an effect from participants carelessly checking answers on one side.

## DISCUSSION

This randomized, double-blind, placebo-controlled experiment investigated the efficacy of echinacea compound herbal tea preparation and whether it decreased the severity of the cold or flu symptoms and how quickly it took effect. We found that treatment with the echinacea compound tea given at early onset of symptoms was effective at relieving cold or flu symptoms in a shorter period of time and was noticeably quicker in number of days until it had an effect than the placebo.

In introducing this study to the staff with the distribution of educational material on echinacea, the intent was that all potential subjects would have the belief that the tea would have an effect. This along with randomization and tight scientific control kept the likelihood of extraneous errors to a minimum. Consequently the differences between the two groups noted on all three measures are more likely to be from the independent variables rather than error or chance.

Subjects were interviewed after the questionnaire was completed; those in the echinacea group reported their acute symptoms of stuffiness, scratchy throat, fever, seemed to subside within a day or two and they were left with merely a "slight drip." The control group, however, reported acute symptoms that lasted 6 to 10 days with little or no relief. Also of interest was the fact that the Rest Haven-York Nursing and Rehabilitation Center experienced 28.7% less absenteeism than the previous year. It is not known whether this is a statistically significant number as it was not tested due to the problem of too many confounding variables (such as severity in different flu and cold seasons, etc.). No side effects were reported by any of the subjects.

A potential limitation of this study is that the sample was not representative of the population. Because of the almost exclusive participation of women in this study, generalization of the results to both a male and female population may be difficult. In addition, there is also the issue of all subjects being in health care and perhaps differing on that basis from the general population. Another shortcoming may be in the alternation of assignment process for

group formation; it was accomplished in this manner for the maintenance of simplicity. Perhaps a survey of the participants would have strengthened the study by determining the effectiveness of the blinding. Because of its simplicity, the questionnaire has some limitations. The purpose of the design was to encourage completion of the survey in all levels of staff (subjects). Choosing an instrument that did not quantify symptoms had an advantage of not confounding the results with extraneous variables such as degrees of cold or flu. Furthermore, self-reporting of cold and flu symptoms and the relief of such have the problems associated with self-report methods.

Further studies are needed to understand better how the benefits of echinacea can best be achieved through type of echinacea, dosage, and timing.

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