Dr Paul Clayton examines the claims of other products:

WHAT ABOUT ECHINACEA?

Echinacea has been in the news lately, due to a series of studies that found it to be ineffective in protecting against respiratory tract infections such as coughs and colds (Grimm & Muller '99, Barrett et al '02, Kreutzfeld '06). These were all randomised, double blind trials with reasonable numbers of trial subjects, so they cannot be lightly dismissed. In addition to these negative findings, three powerful meta-analyses all came to a similar conclusion; Echinacea is ineffective or not proven (Caruso & Gwaltney '05, Carr & Nahata '06, Linde et al '06).

Against this mass of negative data is one meta-analysis that found that Echinacea was effective in preventing symptoms of the common cold (Schoop et al '06). Unfortunately this last study is considerably weaker than the others, as its selection criteria are less stringent. One must also take into account that the study was carried out by and on behalf of A. Vogel Bioforce, a company that sells large quantities of Echinacea products.

However, despite the apparently overwhelming evidence against Echinacea, I personally believe that extracts from this herb can be effective in improving immune function. I have seen a number of cases where Echinacea appeared to be helpful; and although personal experience is of limited scientific value, it can be very persuasive. So why would I set personal experience against the science? Simple; all Echinacea extracts are not the same, and although many are completely useless, some are the real thing.

Echinacea products differ hugely in their composition due to fact that no fewer than three different Echinacea species are used (Echinacea pallida, Echinacea purpurea and Echinacea angustifolia). These species have some pharmacological activities in common, based on the presence in all three of similar active compounds. However, the levels of these compounds differ significantly between the different species (Speroni et al '02, Wolsko et al '05) and even within the same species (Qu et al '05). To make matters worse different manufacturers work with variable and sometimes downright shoddy plant material, use different extraction methods, and frequently add other herbal components to the mix.

Partly because of the lack of standardisation and the complex nature of herbal extracts, Echinacea products have been consistently linked to a low incidence of adverse effects including allergic reactions (Huntley et al '05), ocular problems (Fraunfelder '04), and severe thrombotic thrombocytopenic purpura (George et al '06). This last condition is a true medical emergency, requiring plasma exchange.
There is also data that suggests that Echinacea extracts might reduce male fertility (Ondrizek et al '99), although this is not proven – and could even be desirable.

Echinacea extracts contain a number of compounds that might contribute to the immune-boosting effects so widely claimed for this herb. These include a small number of flavonoids related to caffeic acid (including cichoric acid and echinacoside), an alkamide fraction, and a group of polysaccharide compounds very similar to the beta glucans in yeast (Speroni et al '02, Dalby-Brown et al '05).

Caffeic acid and its derivatives occur in a wide range of foods utterly devoid of any immune-boosting effects, and the alkamides have no reported benefits either. The most reasonable conclusion is that the active compounds in Echinacea are the polysaccharides.

Conclusion:

Echinacea products may be helpful, and they may be completely ineffective. I would be happy to use them in trivial circumstances, but would shy away from them whenever improved immunity was important. Given that standardised yeast extracts are the only products that contain consistently high levels of the critical beta glucan polysaccharides, they are – for me – an automatic first choice instead of Echinacea.

REFERENCES

Barrett BP, Brown RL, Locken K, Maberry R, Bobula JA, D'Alessio D **Treatment of the common cold with unrefined echinacea. A randomized, double-blind, placebo-controlled trial.** Ann Intern Med. 2002 Dec 17;137(12):939-46.

Carr RR, Nahata MC. **Complementary and alternative medicine for upper-respiratory-tract infection in children.** Am J Health Syst Pharm. 2006 Jan 1;63(1):33-9.

Caruso TJ, Gwaltney JM Jr. **Treatment of the common cold with echinacea: a structured review.**Clin Infect Dis. 2005 Mar 15;40(6):807-10.

Dalby-Brown L, Barsett H, Landbo AK, Meyer AS, Molgaard P. **Synergistic antioxidative effects of alkamides, caffeic acid derivatives, and polysaccharide fractions from Echinacea purpurea on in vitro oxidation of human low-density lipoproteins.** J Agric Food Chem. 2005 Nov 30;53(24):9413-23.

Fraunfelder FW. **Ocular side effects from herbal medicines and nutritional supplements.** Am J Ophthalmol. 2004 Oct;138(4):639-47.

George L, Ioannis E, Radostina T, Antonios M. **Severe thrombotic thrombocytopenic purpura (TTP) induced or exacerbated by the immunostimulatory herb Echinacea**. Am J Hematol. 2006 Mar;81(3):224.

Grimm W, Muller 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.

Huntley AL, Thompson Coon J, Ernst E. **The safety of herbal medicinal products derived from Echinacea species: a systematic review.** Drug Saf. 2005;28(5):387-400.

Kreutzfeld B. **Echinacea angustifolia is ineffective in an experimental study**
Med Monatsschr Pharm. 2006 Jan;29(1):39-40.

Linde K, Barrett B, Wolkart K, Bauer R, Melchart D. **Echinacea for preventing and treating the common cold**. Cochrane Database Syst Rev. 2006 Jan 25;(1):CD000530.

Ondrizek RR, Chan PJ, Patton WC, King A. **Inhibition of human sperm motility by specific herbs used in alternative medicine.** J Assist Reprod Genet. 1999 Feb;16(2):87-91.

Qu L, Chen Y, Wang X, Scalzo R, Davis JM. **Patterns of Variation in Alkamides and Cichoric Acid in Roots and Aboveground Parts of Echinacea purpurea (L.) Moench.** HortScience. 2005 Aug;40(5):1239-1242.

Schoop R, Klein P, Suter A, Johnston SL **Echinacea in the prevention of induced rhinovirus colds: a meta-analysis.** Clin Ther.2006 Feb;28(2):174-83.

Speroni E, Govoni P, Guizzardi S, Renzulli C, Guerra MC**. Anti-inflammatory and cicatrizing activity of Echinacea pallida Nutt. root extract**. J Ethnopharmacol. 2002 Feb;79(2):265-72.

Wolsko PM, Solondz DK, Phillips RS, Schachter SC, Eisenberg DM. **Lack of herbal supplement characterization in published randomized controlled trials**. Am J Med. 2005 Oct;118(10):1087-93.

Linde K, Barrett B, Wolkart K, Bauer R, Melchart D. **Echinacea for preventing and treating the common cold**. Cochrane Database Syst Rev. 2006 Jan 25;(1):CD000530.

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BACKGROUND: Preparations of the plant Echinacea (family Compositae) are widely used in some European countries and in North America for common colds. Most consumers and physicians are not aware that products available under the term Echinacea differ appreciably in their composition, mainly due to the use of variable plant material, extraction methods and addition of other components. OBJECTIVES: The objective of this review was to assess whether there is evidence that Echinacea preparations are 1) more effective than no treatment; 2) more effective than placebo; 3) similarly effective to other treatments in A) the prevention and B) the treatment of the common cold. SEARCH STRATEGY: We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library Issue 3, 2005); PubMed (1997 to April 2005), EMBASE (1998 to June 2005), AMED (to August 2005), Centre for Complementary Medicine Research (in Munich) (1988 to May 2005), contacted experts, and screened references of reviews. SELECTION CRITERIA: We included randomized controlled trials that compared mono-preparations of Echinacea with a placebo, no treatment, or another treatment for the prevention or treatment of common colds. Trials on combinations of Echinacea and other herbs were excluded. DATA COLLECTION AND ANALYSIS: For all studies, at least two authors independently assessed eligibility and trial quality, and extracted data. Outcomes of interest in prevention trials were: numbers of individuals with one or more colds, and severity and duration of colds; and in treatment trials: total symptom scores, nasal symptoms, and duration of

colds. MAIN RESULTS: Sixteen trials including a total of 22 comparisons of an Echinacea preparation and a control group (19 with placebo, 2 with no treatment, 1 with another herbal preparation) met the inclusion criteria. All trials except one were described as double-blind. The majority had reasonable to good methodological quality. Three comparisons investigated prevention of colds and 19 comparisons tested treatment of colds. A variety of different Echinacea preparations were used. None of the three comparisons in the prevention trials showed an effect over placebo. Comparing an Echinacea preparation with placebo as treatment, a significant effect was reported in nine comparisons, a trend in one, and no difference in six. More than one trial was available only for preparations based on the aerial parts from Echinacea purpurea (E. purpurea). AUTHORS' CONCLUSIONS: Echinacea preparations tested in clinical trials differ greatly. There is some evidence that preparations based on the aerial parts of Echinacea purpurea might be effective for the early treatment of colds in adults but results are not fully consistent. Beneficial effects of other Echinacea preparations, and for preventative purposes might exist but have not been shown in independently replicated, rigorous randomized trials.

Speroni E, Govoni P, Guizzardi S, Renzulli C, Guerra MC**. Anti-inflammatory and cicatrizing activity of Echinacea pallida Nutt. root extract**. J Ethnopharmacol. 2002 Feb;79(2):265-72.

Among the different species belonging to the Echinacea family, largely used in traditional medicine, Echinacea pallida, Echinacea purpurea and Echinacea angustifolia were investigated. These different species, due to their difficult identification, were commonly confused in the past and probably used indifferently for the same therapeutic purposes. In fact, the three species have in common, some pharmacological activities, based on the presence of active compounds that act additively and synergistically. Nevertheless, the composition of each species has slight variation in the amount of each active component. In particular, echinacoside, a caffeoyl derivative, is present in E. pallida and only in traces in E. angustifolia. It seems to have protective effects on skin connective tissue and to enhance wound healing. The anti-inflammatory and wound healing activities of echinacoside, compared with the ones of the total root extract of E. pallida and E. angustifolia, were examined in rats, after topical application. The tissues of the treated animals were evaluated after 24, 48 and 72 h treatment and excised for histological observation at the end of the experiment. Results confirm the good anti-inflammatory and wound healing properties of E. pallida and of its constituent echinacoside, with respect to E. purpurea and control. This activity probably resides in the antihyaluronidase activity of echinacoside.

Dalby-Brown L, Barsett H, Landbo AK, Meyer AS, Molgaard P. **Synergistic antioxidative effects of alkamides, caffeic acid derivatives, and polysaccharide fractions from Echinacea purpurea on in vitro oxidation of human low-density lipoproteins.** J Agric Food Chem. 2005 Nov 30;53(24):9413-23.

Preparations of Echinacea are widely used as alternative remedies to prevent the common cold and infections in the upper respiratory tract. After extraction, fractionation, and isolation, the antioxidant activity of three extracts, one alkamide fraction, four polysaccharide-containing fractions, and three caffeic acid derivatives from Echinacea purpurea root was evaluated by measuring their inhibition of in vitro Cu(II)-catalyzed oxidation of human low-density lipoprotein (LDL). The antioxidant activities of the isolated caffeic acid derivatives were compared to those of echinacoside, caffeic acid, and rosmarinic acid for reference. The order of antioxidant activity of the tested substances was cichoric acid > echinacoside > or = derivative II > or = caffeic acid > or = rosmarinic acid > derivative I. Among the extracts the 80% aqueous ethanolic extract exhibited a 10 times longer lag phase prolongation (LPP) than the 50% ethanolic extract, which in turn exhibited a longer LPP than the water extract. Following ion-exchange chromatography of the water extract, the majority of its antioxidant activity was found in the latest eluted fraction (H2O-acidic 3). The antioxidant activity of the tested Echinacea extracts, fractions, and isolated compounds was dose dependent. Synergistic antioxidant effects of Echinacea constituents were found when cichoric acid (major caffeic acid derivative in E. purpurea) or echinacoside (major caffeic acid derivative in Echinacea pallida and Echinacea angustifolia) were combined with a natural mixture of alkamides and/or a water extract containing the high molecular weight compounds. This contributes to the hypothesis that the physiologically beneficial effects of Echinacea are exerted by the multitude of constituents present in the preparations.