P.O. Box 144345 Austin, TX 78714-4345 ▪ 512.926.4900 ▪ Fax: 512.926.2345 ▪ www.herbalgram.org

HerbClip™

FILE: ▪ Echinacea (*Echinaceae purpurea*)
▪ Immunity
▪ Esberitox®
▪ Lymphocytes

HC 090151-289

Date: September 30, 2005

RE: Immunomodulatory Effects of *Echinaceae purpurea* root

Schwarz E, Parlesak A, Henneicke-von Zepelin HH, Bode JC, Bode C. Effect of administration of freshly pressed juice of *Echinacea purpurea* on the number of various subpopulations of B- and T-lymphocytes in healthy volunteers: results of a double-blind, placebo-controlled cross-over study. *Phytomed.* 2005;12:625-631.

Echinacea-containing herbal preparations have become increasingly popular over the past two to three decades as immunomodulatory agents and are currently one of the best-selling herbal preparations in the United States. The results of many uncontrolled and controlled clinical trials strongly suggest that echinacea-containing products "ameliorate the symptoms and shorten the duration of colds and upper respiratory infections," even though some trials have turned out negative, showing no measurable benefits for some echinacea preparations. Nearly all echinacea-containing products are formulated for oral use. However, there is some conjecture as to whether certain constituents of preparations made from parts of this herb may not be absorbed by the intestinal mucosa or might be destroyed during the digestive process when it is taken orally, which would eliminate its immunomodulatory effect. Therefore, the objective of this study was to clarify whether phagocytic activity and cytokine production are stimulated by the oral administration of a commercially available *Echinacea purpurea* preparation (EPP) containing materials from the roots of *E. purpurea*.

Forty healthy men aged 20–40 years were enrolled in this double-blind, placebo-controlled, crossover study, which consisted of two 14-day treatment periods separated by a 14-week washout period and took place in Germany. The participants ingested 12 mL of either a freshly pressed juice of echinacea root (Esberitox® Mono of Schaper & Brümmer, Salzgitter, Germany) or placebo juice daily. (This company also makes another product called Esberitox® which contains ethanolic extracts of the following herbs: wild indigo [*Baptisia tinctoria*] root; 32 mg; *E. purpurea* and *pallida* 1:1, 22.5 mg; thuja [*Thuja occidentalis*] leaf; 6 mg) or placebo juice daily. Venous blood was collected in the morning on days 0, 7, 14 of the first treatment period and on days 42, 49, and 56 of the second treatment period. A flow cytometer was used to measure the total number of lymphocytes and of 12 lymphocyte subpopulations within 1 hour of sampling.

EPP treatment for 1 and 2 weeks did not significantly increase the concentrations of T- and B-lymphocytes or of CD4+ and CD8+ T lymphocytes, including the subgroups of naïve and memory lymphocytes and natural killer cells. The only significant changes ($P < 0.05$) observed after 1 week of EPP treatment were small decreases in the total lymphocyte count (–6%) and in the subgroup of CD8+ lymphocytes expressing CD45-RA (–8.8%). The only significant ($P < 0.05$) change observed after 2 weeks of treatment was a decrease in the mean number of CD4+ T lymphocytes expressing CD45-RA in both the EPP (–7.4%) and the placebo (–8.6%) groups.

The small changes observed in this design protocol were considered to be of "questionable biologic relevance." Furthermore, the results indicate "no evidence of an Echinacea-induced increase in any of the lymphocyte subpopulations investigated." It is thought that what some authors term the previously observed "immunostimulatory" (many herb experts have indicated a preference for the term "immunomodulatory", as use above) effects of echinacea preparations in vitro and after parenteral application were caused by direct contact of the constituents with the cells of the immune system being investigated. The authors recommend that additional studies should be conducted to determine the mechanisms responsible for the previously observed beneficial effects of echinacea preparations to treat or prevent upper respiratory tract infections in clinical studies.

Interestingly, they found a slight decrease of the total number of lymphocytes in their peripheral blood samples. However, they did not discuss this in the light of the findings of Parham et al.[1] and Rösler et al.[2] Accordingly, the slight decrease of the cell number in the central compartment may be due to a homing of activated cells to the Mucosa-Associated-Lymphatic-Tissue (MALT), Bronchial-ALT (BALT), or Gastrointetinal-ALT (GALT).

An in vitro pharmacological study was recently conducted by Gertsch et al.[3] These authors attempted to elucidate the molecular mechanism of action of a standardized *E. purpurea* root extract preparation (Echinaforce™; A. Vogel Bioforce AG, Switzerland) that was previously shown to have a "significant benefit in the treatment of the common cold." The results of that study indicated that the major alkylamide constituents of the preparation (i.e., dodeca-2*E*,4*E*,8*Z*,10*E*/*Z*-tetraenoic acid isobutylamides and trienoic and dienoic acids) were the bioactive principles responsible for the beneficial effect.

—Brenda Milot, ELS

Reference

[1]Parnham MJ. Benefit-risk assessment of the squeezed sap of the purple coneplower (Echinacea purpurea) for long-term oral immunostimulation, Phytomedicine 1996;3:95-102.
[2]Rösler J, et al. Application of purified polysaccharides from cell cultures of the plant Echinacea purpurea to test subjects mediates activation of the phagocyte system, Int J Immunopharmac 1991;13:931-941
[3]Gertsch J, Schoop R, Kuenzle U, Suter A. *Echinacea* alkylamides modulate TNF-α gene expression via cannabinoid receptor CB2 and multiple signal transduction pathways. *FEBS Lett*. 2004;577:563–569.

Enclosure: Referenced article reprinted with permission from Elsevier, GmbH.