Effects of Echinaforce® treatment on ex vivo stimulated blood cells

Study objective  The efficacy of Echinacea purpurea to prevent and treat colds and flu-like infections is based on modulatory effects on the immune system. It is largely unknown how this modulation manifests in vivo, and how the effects develop in subjects with a higher susceptibility to colds or low immune response. The goal of this study was to monitor several immune mediators during Echinacea treatment using an ex vivo stimulation model [1].

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Herbal extract  A standardised alcohol extract of fresh herb (95 %) and roots (5 %) of the traditional medicinal plant Echinacea purpurea (L.) Moench (Echinaforce®, A.Vogel Bioforce AG, Switzerland).

Study design  A total of 30 healthy subjects who reported having two or more common colds a year were included in the study (12 women, 18 men; aged: 18-57). Individual stress levels were assessed using the perceived stress score-10 questionnaire (PSS-10). During the study common cold symptoms were to be recorded in a diary. After a run in phase of two days (baseline) subjects began to take a daily oral dose of 4 x 1 ml Echinaforce® over five days followed by 10 x 1 ml over three days. During this ten-day study phase blood samples were taken from the subjects every day and any side effects were noted.

Ex vivo stimulation  Daily blood samples were subjected to ex vivo stimulation with standardised immune stimulants. Afterwards the serum was tested for elastase, interleukin-1β (IL-1β), IL-6, IL-8, IL-10, IL-12, MCP-1 (monocyte chemotactic protein-1), tumour necrosis factor-α (TNF-α) and interferon-γ (IFN-γ). All immune parameters were measured at baseline (day 1 and 2) and then for every treatment day. All changes were analysed and classified according to subject characteristics (stress-level, susceptibility to cold infections or immune response at baseline).

Results

Subjects  The mean age of the 30 subjects was 24.1 years, the mean weight 67.7 kg, the mean height 171.4 cm and the mean body mass index 23. The data of two subjects could not be used due to violation of the study protocol. Symptoms of common cold were not noted by any of the participants. The differential blood count also showed no clinically relevant changes for the entire period of time.

Overall effects  Compared to the baseline values, the synergistically active, pro-inflammatory cytokines IL-1β and TNF-α had significantly decreased by up to 24 % (p<0.05) while at the same time the level of anti-inflammatory cytokines IL-10 had significantly increased by 13 % (p<0.05). Likewise, the production of IL-8 and MCP-1 at ex vivo stimulation had increased by around 25 % each (p<0.05) following treatment with echinacea. Thus the treatment produced significant anti-inflammatory effects and induction of chemotactic activities.
Adaptive effects (sub-groups) Subjects whose immune cells showed initial “weak” immune reaction experienced exceptionally pronounced effects upon treatment: In subjects with a low production of IFN-γ, IL-8, IL-10 and MCP-1 at baseline, *Echinacea* treatment induced significant additional formation of these signal substances (18 %, 35 %, 28 %, 49 %; p<0.05 in each case). In contrast, there was no further increase in subjects with a high initial formation of these factors at baseline (Figure 1). Subjects with high initial titres of TNF-α and IL-1ß were found to have decreased levels of these mediators from the very first day of medication on.

These adaptive *Echinacea* effects were also demonstrated when subjects were classified according to their exposure to stress or their susceptibility to cold infections. In stressed subjects, the IFN-γ titre rose by 25 % under *Echinacea* treatment (temporarily up to 50 % when the dose was raised for one day). A similar IFN-γ induction was seen in subjects with increased susceptibility to cold infection. Only in subjects with low initial cortisol levels, *Echinacea* caused a significant reduction in acute phase proteins (IL1-ß, IL-6, IL-12, TNF-α).

**Safety** While taking *Echinacea* subjects did not report any undesirable effects at low or high doses. Only slight reddening at the injection site was observed. There were also no changes in the blood cell count (leukocytes for example) nor any clinically relevant alterations in metabolic parameters such as GGT, bilirubin and various lipid values.

**Conclusion**

This is the first clinical study to systematically investigate the effects of repeated Echinaforce® applications, on a series of immune mediators. It is also the first approach to allocate the effects to immunological conditions in the treated subjects. Overall, the fresh *Echinacea* extract Echinaforce® reduces inflammatory processes and increases leukocyte chemotaxis. Activation of antiviral defences appears in subjects with higher stress levels and/or susceptibility to colds. A general support of immune reactions is observed in participants with a weak immune performance and initial low immune mediators. The authors chose the term “adaptive immune modulation” to describe the selective effects of *Echinacea* on subjects with weak immune responses and in those with greater susceptibility to infections and increased pressure at work or at home.

![Figure 1](image-url) The chemokine, monocytes-chemotactic-protein-1 (MCP-1), recruits and stimulates numerous immune cells relevant for viral clearance (monocytes or natural killer cells).

In subjects with low initial cytokine production (red line) *Echinacea* caused a highly significant increase in MCP-1 concentration, but not in subjects with an already high initial cytokine production (blue line).

For reasons of comprehensibility, error bars were not indicated in the graphic.