

J Med Food

. 2007 Sep;10(3):423-34.

doi: 10.1089/jmf.2006.257.

Enhancement of innate and adaptive immune functions by multiple Echinacea species

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Comparative Study

Enhancement of innate and adaptive immune functions by multiple Echinacea species

Zili Zhai et al. J Med Food. 2007 Sep.

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Abstract

Echinacea preparations are commonly used as nonspecific immunomodulatory agents. Alcohol extracts from three widely used Echinacea species, *Echinacea angustifolia*, *Echinacea pallida*, and *Echinacea purpurea*, were investigated for immunomodulating properties. The three Echinacea species demonstrated a broad difference in concentrations of individual lipophilic amides and hydrophilic caffeic acid derivatives. Mice were gavaged once a day (for 7 days) with one of the Echinacea extracts (130 mg/kg) or vehicle and immunized with sheep red blood cells (sRBC) 4 days prior to collection of immune cells for multiple immunological assays. The three herb extracts induced similar, but differential, changes in the percentage of immune cell populations and their biological functions, including increased percentages of CD49+ and CD19+ lymphocytes in spleen and natural killer cell cytotoxicity. Antibody response to sRBC was significantly increased equally by extracts of all three Echinacea species. Concanavalin A-stimulated splenocytes from *E. angustifolia*- and *E. pallida*-treated mice demonstrated significantly higher T cell proliferation. In addition, the Echinacea treatment significantly altered the cytokine production by mitogen-stimulated splenic cells. The three herbal extracts significantly increased interferon-alpha production, but inhibited the release of tumor necrosis factor-gamma and interleukin (IL)-1beta. Only *E. angustifolia*- and *E. pallida*-treated mice demonstrated significantly higher production of IL-4 and increased IL-10 production. Taken together, these findings demonstrated that Echinacea is a wide-spectrum immunomodulator that modulates both innate and adaptive immune responses. In particular, *E. angustifolia* or *E. pallida* may have more anti-inflammatory potential.

Figures

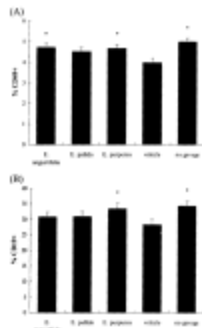


FIG. 1

5

Effect of *Echinacea* preparations on...

FIG. 1

13

Effect of *Echinacea* preparations on the percentages of (A) splenic CD49+ and (B)...

FIG. 1

Effect of *Echinacea* preparations on the percentages of (A) splenic CD49+ and (B) CD19+ subsets. Male BALB/c mice were orally administered one of three *Echinacea* preparations, 130 mg/kg daily for 7 consecutive days. The vehicle control mice received an equal volume of 5% ethanol vehicle. Spleen cells were isolated to analyze the expression of the CD49 (NK cell subset) and CD19 (B-cell subset) markers by flow cytometry as described in Materials and Methods. Results are presented as mean \pm SE values of two independent experiments ($n = 6$). *Significant group difference from vehicle control at $P < .05$.

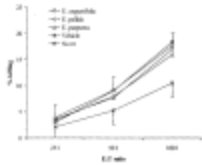


FIG. 2

5

Effect of *Echinacea* preparations on...

FIG. 2

13

Effect of *Echinacea* preparations on NK cytotoxicity after covarying for the percentage of...

FIG. 2

Effect of *Echinacea* preparations on NK cytotoxicity after covarying for the percentage of CD49+ splenocytes in each animal. NK cell cytotoxicity was measured as described in Materials and Methods and expressed as percentage cytolysis of target cells. Results are presented as mean \pm SE values of two independent experiments ($n = 6$). E:T, effector:target cell ratio; trt, treatment.

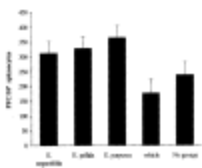


FIG. 3

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Effect of *Echinacea* preparations on...

FIG. 3

13

Effect of *Echinacea* preparations on splenic PFC response after covariance for the percentage...

FIG. 3

Effect of *Echinacea* preparations on splenic PFC response after covariance for the percentage of CD19+ splenocytes in each animal. PFC response was assayed as described in Materials and Methods and expressed as PFCs per 10^6 splenocytes. Results are presented as mean \pm SE values of two independent experiments ($n = 6$).

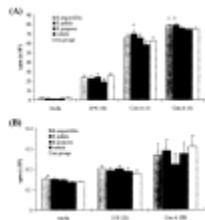


FIG. 4

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Effect of *Echinacea* preparations on...

FIG. 4

13

Effect of *Echinacea* preparations on (A) splenic and (B) blood lymphocyte proliferation. The...

FIG. 4

Effect of *Echinacea* preparations on (A) splenic and (B) blood lymphocyte proliferation. The lymphocyte proliferation assay was conducted as described in Materials and Methods. Results were expressed as cpm (^3H incorporation) $\times 10^3$ and are presented as mean \pm SE values of two independent experiments ($n = 6$). Numbers in parentheses are the concentration of each mitogen (in $\mu\text{g}/\text{mL}$). *Significant difference from vehicle control at $P < .05$.

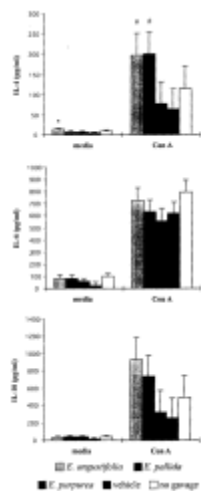


FIG. 5

Effect of *Echinacea* preparations on...

FIG. 5

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Effect of *Echinacea* preparations on T_H2 cytokine production by mouse splenocytes...

FIG. 5

Effect of *Echinacea* preparations on T_H2 cytokine production by mouse splenocytes stimulated *in vitro* without or with mitogen. Spleen cells were incubated without or with Con A at 10 µg/mL for 72 hours. Cytokine levels were determined as described in Materials and Methods. Results are presented as mean ± SE values of two independent experiments (*n* = 6). *Significant difference from vehicle control at *P* < .05. #Significant difference for the combination of corresponding *Echinacea* treatment groups from vehicle control.

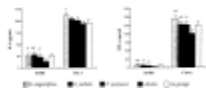


FIG. 6

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Effect of *Echinacea* preparations on...

FIG. 6

13

Effect of *Echinacea* preparations on T_H1 cytokine production by mouse splenocytes stimulated...

FIG. 6

Effect of *Echinacea* preparations on T_H1 cytokine production by mouse splenocytes stimulated *in vitro* without or with mitogen. Spleen cells were incubated without or with Con A at 10 µg/mL for 48 hours. Cytokine levels were determined as described in Materials and Methods. Results are presented as mean ± SE values of two independent experiments (*n* = 6). *Significant difference from vehicle control at *P* < .05. #Significant difference for the combination of corresponding *Echinacea* treatment groups from vehicle control.

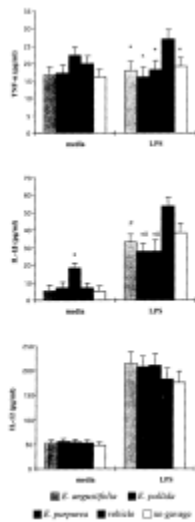


FIG. 7

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Effect of *Echinacea* preparations on...

FIG. 7

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Effect of *Echinacea* preparations on macrophage cytokine production *in vitro* without or with...

FIG. 7

Effect of *Echinacea* preparations on macrophage cytokine production *in vitro* without or with mitogen. Spleen cells were incubated without or with LPS at 10 $\mu\text{g}/\text{mL}$ for 24 hours at 37°C in a 7% CO₂ incubator. Cytokine levels were determined as described in Materials and Methods. Results are presented as mean \pm SE values of two independent experiments ($n = 6$). *Significant difference from vehicle control at $P < .05$. #Significant difference for the combination of corresponding *Echinacea* treatment groups from vehicle control.

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