Phytomedicine

Study Summary June 2010

Echinacea Extract: Bactericidal and Immunomodulatory for Clinically Relevant Pathogens of Respiratory Tract *Infections*[1]

Study aim: The traditional medicinal plant Echinacea has effects that go far beyond systemic immune stimulation as previously assumed. For example, distinct antiviral, infection-blocking [2] and immunomodulating effects [3]. The aim of the study was to therefore investigate *in vitro* whether Echinacea also has direct antibacterial effects and can normalise proinflammatory cytokines that are released during bacterial infections [1].

Researchers involved: Dr. *Manju Sharma* and Prof. Dr. *James B. Hudson*, Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, Canada; Dr. *M. Anderson*, Prostate Centre, General Hospital Vancouver, Canada; Dr. *Roland Schoop*, A.Vogel Bioforce AG, Roggwil, Switzerland.

Plant extract: Different concentrations of a standardised alcoholic extract of fresh herb (95%) and roots (5%) of the traditional medicinal plant *Echinacea purpurea* (L.) Moench (Echinaforce®, A.Vogel Bioforce AG, Switzerland) were tested.

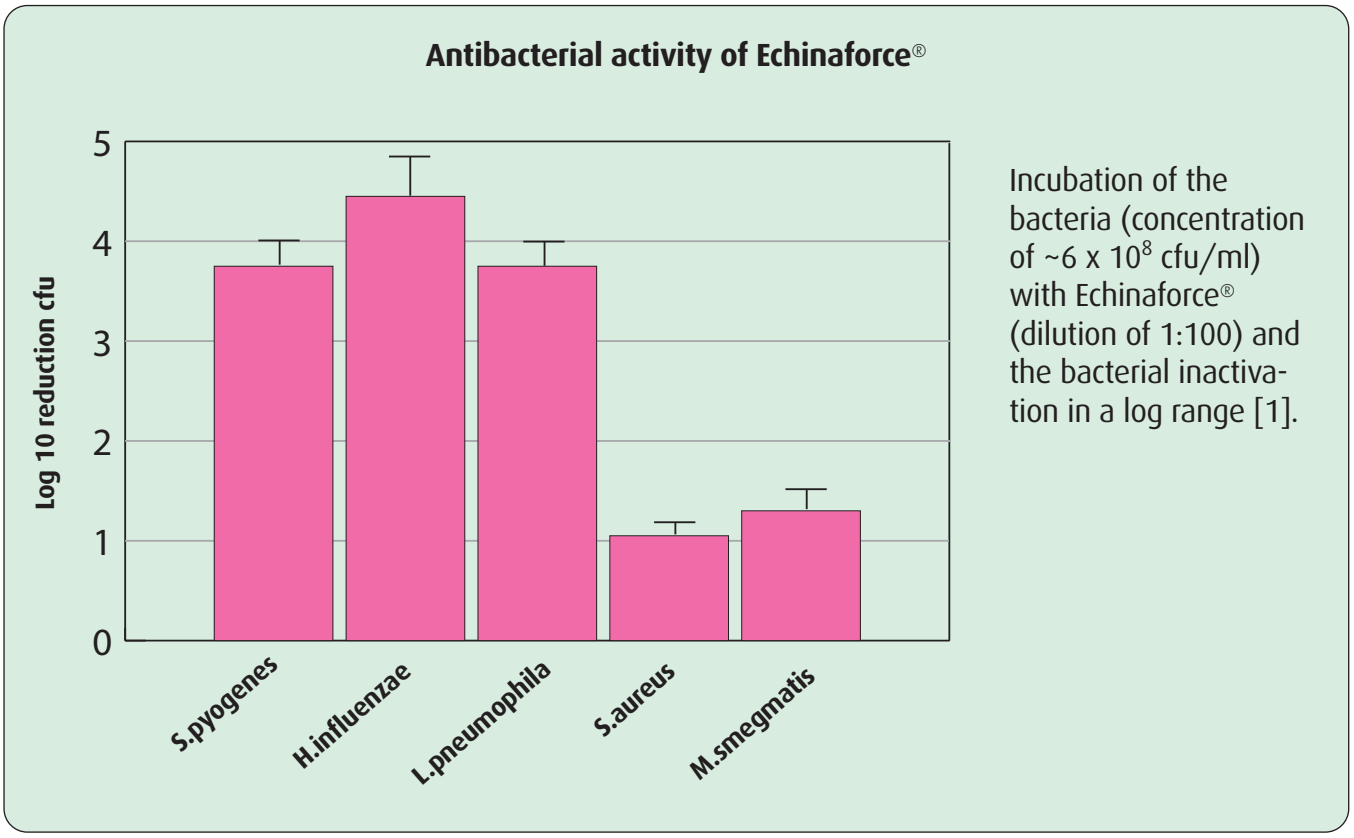
Test material/experiment setup: The bactericidal effect of the extract was tested with common bacterial pathogens (*Acinetobacter baumannii, Bacillus cereus, Bacillus subtilis, Enterococcus faecalis* (vancomycin resistant), *Escherichia coli, Haemophilus influenzae, Klebsiella pneumoniae, Legionella pneumophila, Mycobacterium smegmatis, Pseudomonas aeruginosa, Staphylococcus aureus* (methicillin resistant and sensitive, respectively), *Streptococcus pyogenes*). In addition, the sensitivity of the fungi *Candida albicans* and *Trichoderma viride* was tested. The cytokine analyses were performed with two well-established cell lines for this purpose (BEAS-2B – bronchial epithelial cells, A-549 – lung epithelial cells). Cytokine detection followed with both ELISA (IL-6, IL-8, TNF-α) and with a novel cytokine antibody array (20 cytokine and inflammation-relevant mediators).

Results

→ Antibacterial effects: Differences in the bactericidal effect were pathogen-dependent. Typical agents of respiratory diseases and complications *S. pyogenes, H. influenzae* and *L. pneumophila* were completely deactivated by the Echinacea extract at dilutions of 1:100 or less (equivalent to <160 µg/ml dry mass). The achieved bacterial inactivation was 4 logs (99.99%) and more. The bactericidal effect of the extract tested was dose dependent, whereby higher concentrations (1:100) completely inactivated Echinacea-sensitive bacteria. However, with high dilutions of 1:400, Echinacea still had a substantial antibacterial effect. With an inactivation of 1 log (90%), *S. aureus* and *M. smegmatis* were less sensitive to the medicinal plant extract. Since, however, Echinacea will be used at far higher concentrations in the field, clinical relevance could even be ascribed to these effects (e.g. in local treatment). With other bacterial pathogens and with the fungi tested, purple coneflower extract had a low bactericidal (less than 1 log (< 90%) bacterial inactivation) or lack of fungicidal effect, respectively.

[1] S.M. Sharma a, M.Anderson b, S.R.Schoop c, J.B.Hudson: Bactericidal and anti-inflammatory properties of a standardized Echinacea extract (Echinaforce®): Dual actions against respiratory bacteria. Phytomedicine. 2010 July; 17(8-9): 563-8 (DOI:10.1016/j.phymed.2009.10.022).
[2] Pleschka S, Stein M, Schoop R, Hudson JB: Anti-viral properties and mode of action of standardized Echinacea purpurea extract against highly pathogenic avian influenza virus (H5N1, H7N7) and swine-origin H1N1 (S-OIV). Virol J. 2009 Nov 13;6:197 (DOI: 10.1186/1743-422X-6-197).
[3] Sharma M, Anderson SA, Schoop R, Hudson JB: Induction of multiple pro-inflammatory cytokines by respiratory viruses and reversal by standardized Echinacea, a potent antiviral herbal extract. Antiviral Res. 2009 Aug;83(2):165-70 (DOI: 10.1016/j.antiviral.2009.04.009).
[4] Brundage JF, Shanks GC. Deaths from bacterial pneumonia during 1918-1919 influenza pandemic. Emerg Infect Dis. 2008 Aug;14(8):1193-9.

Note: The standardised Echinacea plant extract investigated complies with the use of raw materials, manufacture and composition with regard to the product Echinaforce® (A.Vogel Bioforce AG, Roggwil, Switzerland).



Incubation of the bacteria (concentration of ~6 x 10^8 cfu/ml) with Echinaforce® (dilution of 1:100) and the bacterial inactivation in a log range [1].

→ Cytokine release: The infection of the cell cultures tested, for example, with *S. pyogenes*, generally led to the release of significant amounts of proinflammatory mediators, such as IL-6, IL-8, MCP-1, GM-CSF or GRO-α and, to a lesser extent, IL-4 and MIP-1α. In uninfected untreated cells, elevated release of such pro-inflammatory signal substances was not found. Treatment of bacterially infected cell cultures with Echinacea completely prevented the release of all infection mediators tested. This effect on infection-related cytokine release by purple coneflower treatment was largely similar with all bacterial pathogens tested: Echinacea could effectively block release of mediators in all cases. And, in fact, independently of how pronounced the bactericidal effect of Echinacea on the bacteria was. Thus cytokine release — despite the low bactericidal effect on *S. aureus* — was normalized after *S. aureus* infection by the medicinal plant extract, even with the methicillin-resistant strains (MRSA).

Conclusion

Bacterial exacerbation ("superinfection") of most virally caused colds is medically important, particularly in patients with pre-existing conditions, for example, with chronic bronchitis or COPD. The symptoms of bacterial superinfection limit the vitality, the quality of life or the ability to work in millions of people with colds. Bacterial superinfections may lead to the substantial protraction of trivial colds. In the past, bacteria such as *Haemophilus influenzae* or *Streptococcus pneumoniae* caused increased lethality of initial viral infections such as the Spanish flu [4]. The study presented shows that the standardized Echinacea fresh plant extract could influence bacterial infections in two ways. On the one hand through a direct and specific effect against important bacterial pathogens of upper respiratory tract infections. And on the other hand through modulation of proinflammatory signal substances caused by bacteria, which can normalize illnesses caused by inflammation.

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