VIROLOGY JOURNAL

Study Summary (accepted for publication November 2009)

Antiviral properties of *Echinacea Purpurea* against Influenza virus H5N1, H7N7 and H1N1 *in vitro*

Study objective

Recent studies suggest that a specific Echinacea extract has direct antiviral activity against a wide range of respiratory tract viruses including influenza. [2]. Because of pandemic influenza (new influenza, "swine flu") the question arises whether innovative findings of phytotherapeutic research can offer complementary treatment options of the kind urgently called for by the WHO. A international team of research scientists has therefore now investigated whether a standardised Echinacea purpurea extract also has antiviral activity in an in vitro infection model against human pathogenic influenza viruses with pandemic potential. Another focus of interest is which molecular mechanisms of action could be responsible for these effects.

Researchers involved

Prof. Dr. *Stephan Pleschka* and Dr. *Michael Stein*, Institute for Medical Virology, Justus-Liebig University, Giessen, Germany; Prof. Dr. *James B. Hudson*, Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, Canada.

Plant extract

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

In vitro infection model

Besides the seasonal influenza pathogen (H3N2), further novel influenza A strains were investigated: human pathogenic, avian H5N1 and H7N7 and porcine H1N1 are infectious and pathogenic to differing degrees. All have a potential to trigger pandemics. Renal epithelial cells (MDCK cells) were infected with the viral strains. The Echinacea extract was added to the cell cultures at different times and in varying concentrations and the degree of infection inhibition was then determined.

Results

Marked inhibition of infectiousness

The Echinacea extract inhibits influenza viruses H3N2, H5N1, H7N7(bird flu) and H1N1 (swine flu) significantly. Fig. 1. The needed IC=inhibitory concentration was between 1.6 µg/ml to 50 µg/ml and is herewith by far below the recommended dosage for oral treatment. The inhibiting effect remained unchanged even with high virus concentrations (e.g.10^5 PFU/ml).

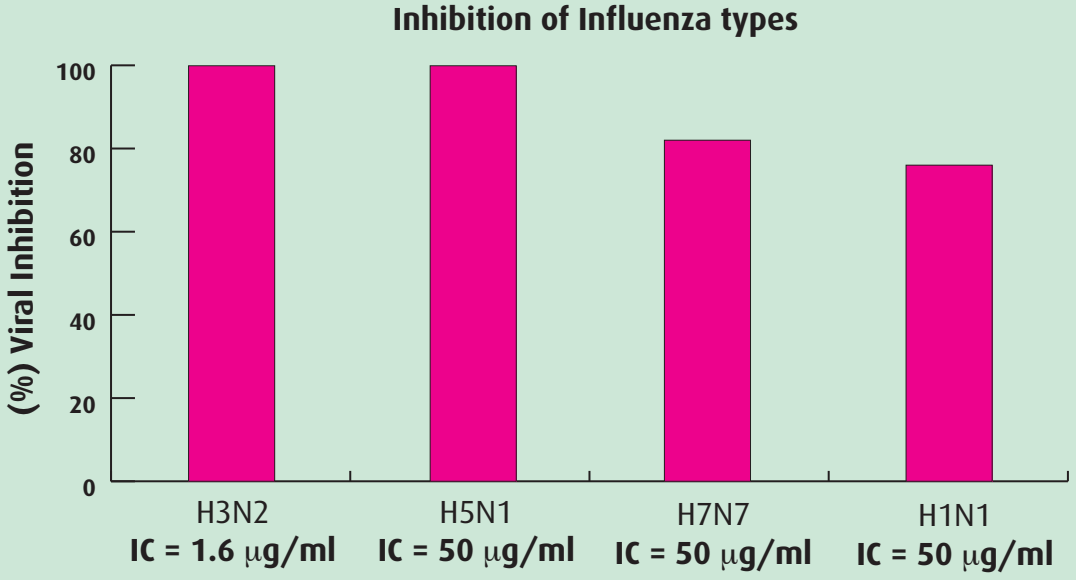

Fig. 1:
The Echinacea extract inhibits all studied influenza types to equal extent.

No development of resistance

Upon treatment with Echinacea extract no resistant virus strains emerged, not even after several rounds of treatment cycles (see Figure 2, second bar of each cycle). In contrast, 87% of the viruses were already resistant to the antiviral substance oseltamivir after the second treatment cycle (see Figure 2, third bar of each cycle), and almost 100% after the third cycle.

Activity against Oseltamivir resistant viruses

The influenza strains that were almost completely resistant after multiple treatment with oseltamivir (see Figure 2, third treatment cycle, third bar), were finally treated with Echinacea. The plant extract inhibited the infectiousness of the oseltamivir-resistant influenza viruses to more than 99.9%.

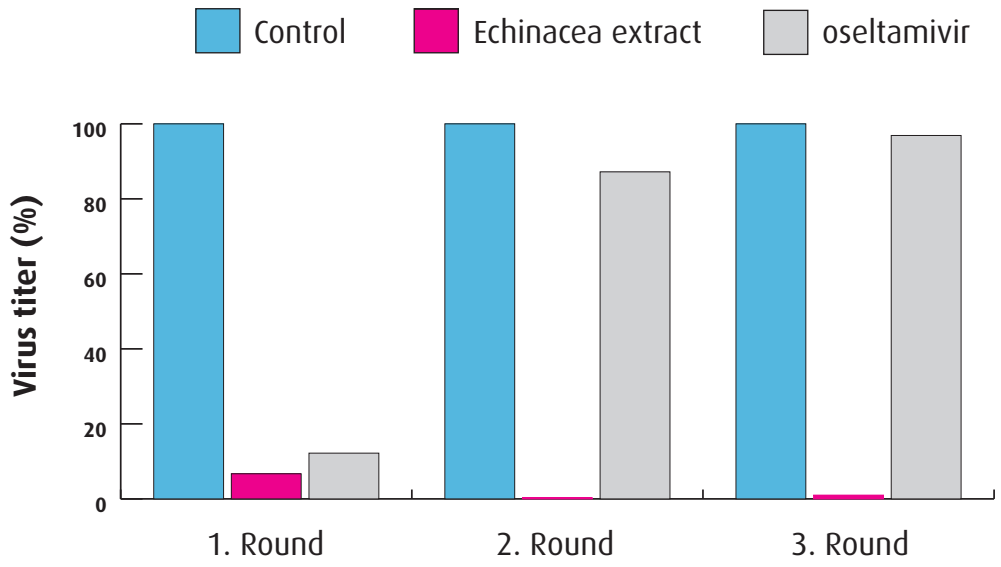

Fig. 2:
The emergence of resistant viruses while treated with Echinaforce and oseltamivir. The figures show the degree of infectiousness of resistant viruses.

Molecular mechanism of the antiviral action

The studies on the molecular mechanism of action suggested that the Echinacea extract investigated exerts its antiviral activity by acting directly on the viruses at a very early stage in the infectious cycle. Even before the infection of the epithelial cells, Echinacea changes the viral surface protein hemagglutinin essential for the viruses to dock onto cells. Consequently, viral adhesion to cell receptors is interrupted. The influenza cells can then no longer penetrate into and replicate inside cells.

Conclusion

The results presented emphasise that the Echinacea fresh plant extract used in the study also exerts antiviral activity against clinically relevant influenza viruses in the *in vitro* infection model, including viruses with pandemic potential.

The central factor for achieving this effect appears to be an early exposure of the viruses to the extract. Especially viral hemagglutinin is altered thereby blocking an important step in the infectious cascade. The antiviral effect already occurs at well below the extract concentrations used for oral treatment. No viral resistances to Echinacea have been observed. Viruses that have become resistant to oseltamivir continue to be sensitive to Echinacea.

The degree of *in vivo* effectiveness of Echinaforce® against pandemic influenza infections is the subject of planned clinical research. The authors of the study draw attention to the fact that Echinaforce® as a standard preparation is a useful, readily available, reasonably priced and clinically relevant supplement to recommended standard options for influenza control.

[1] 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). Virology Journal (paper accepted November 2009).
[2] 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 (http://dx.doi.org/10.1016/j.antiviral.2009.04.009).

Note: The studied standardised Echinacea plant extract corresponds in the raw materials used, manufacture and composition with the product Echinaforce® (A.Vogel Bioforce AG, Roggwil, Switzerland).