



CONFERENCE REPORT

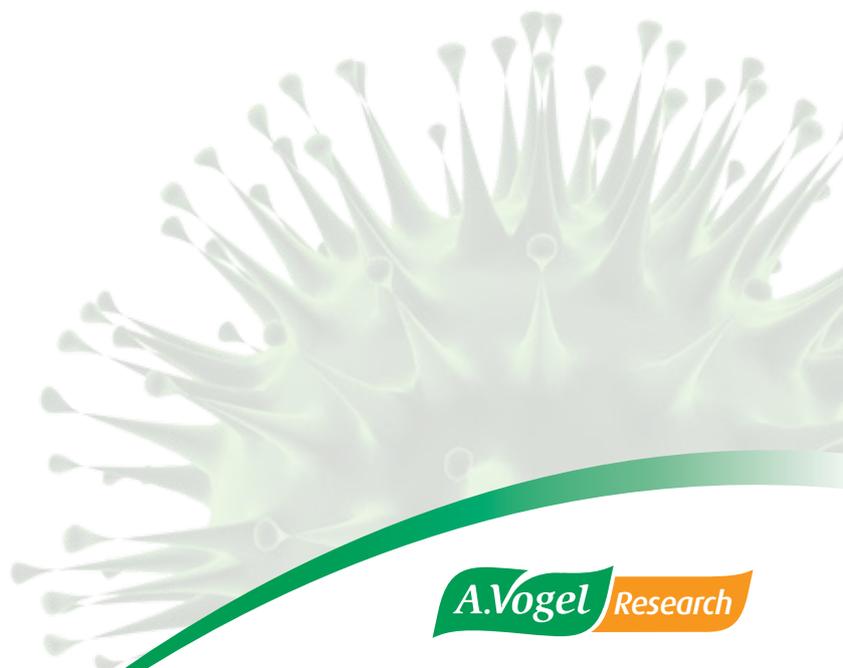
Echinacea

Exploring New Therapeutic Options

Royal Society of Medicine

London (UK)

22nd May 2015



A.Vogel Research

Introduction

Despite advances in modern medicine, the respiratory tract infections (RTIs) we refer to as colds and flu are still extremely prevalent ⁽¹⁾.

Viruses are at the centre of almost every RTI. Over 200 different pathogens are now known and some, such as influenza or coronaviruses, are highly virulent, having the potential to induce tissue damage and inflammation in the airways ^(2,3). These infections can also present a substantial challenge to the immune system (Figure 1).

Studies have shown that up to 20% of cold and flu infections lead to complications such as pneumonia, bronchitis or sinusitis ⁽⁴⁾. These are common reasons for the use of antibiotics in primary healthcare, desperately prescribed because of lack of therapeutic alternatives, but with consequences for increasing bacterial antibiotic resistance ⁽⁵⁾.

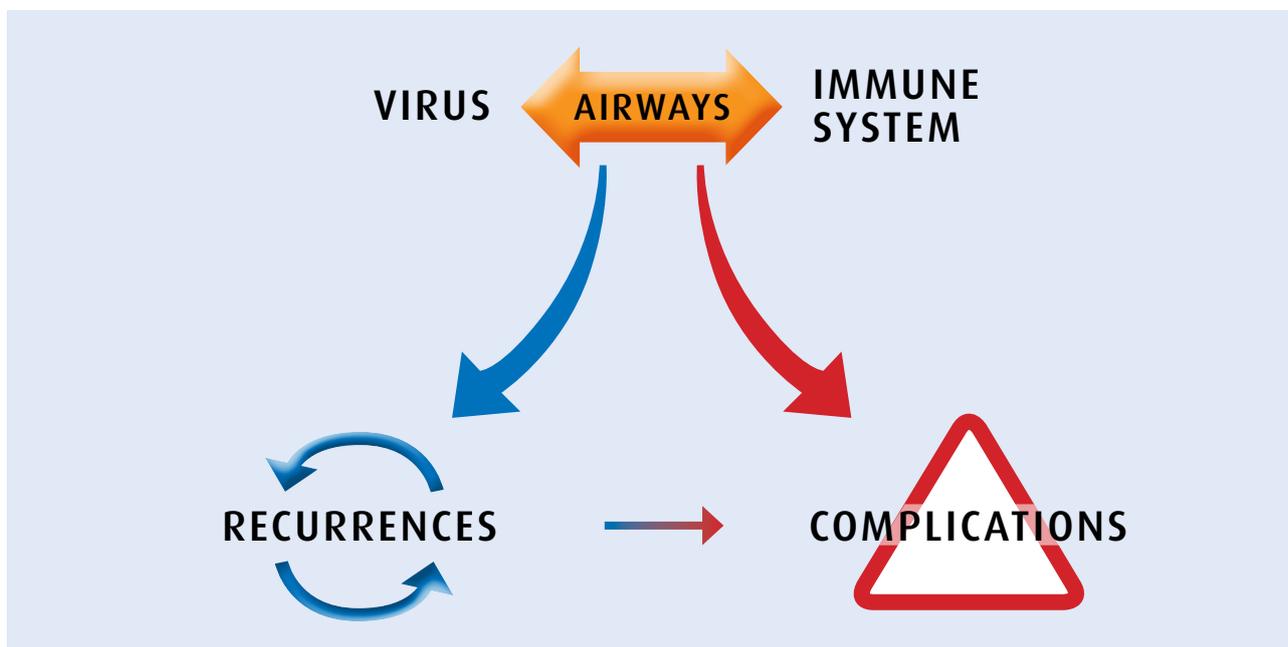


Figure 1: Respiratory Tract Infections are the symptomatic manifestation of viruses interacting with the immune system. Respiratory viruses primarily attack the airways making them susceptible to recurrences and complications.

To date, no treatment has been shown to prevent unfavourable progression of RTIs and the risk of developing complications. Neuraminidase inhibitors such as Oseltamivir and vaccines target only a few in the vast array of respiratory viruses and moreover, are not available for self-medication in early treatment.

Many with colds and flu rely on self-medication with proprietary products containing paracetamol and ibuprofen for symptom relief. However, recent research has shown that these may have the potential to increase the risk of complications and re-consultation probably because of partial immune suppressive effects ⁽⁶⁾.

Echinacea purpurea has long been used to support the immune system and in addition, recent studies have found a broad and direct antiviral activity even against highly pathogenic viruses such as influenza, coronavirus and respiratory syncytial viruses, some of which are well-known factors in the development of complications.

In this conference, we asked whether Echinacea could fill an important gap in the therapeutic arsenal and provide a solution for the prevention of recurrent infections and complications arising from the common cold or flu. We also compared the efficacy of Echinacea with a standard synthetic agent recommended for the treatment of acute influenza infections.

Antiviral Activity of Echinaforce®

Dr. Oliver Engler, Federal Office for Civil Protection, Spiez Laboratory, Switzerland

Dr. Selvarani Vimalanathan, University of British Columbia, Canada

The recent past has seen the emergence of SARS and MERS coronaviruses, and antigenically shifted influenza viruses such as H1N1pdm09 and H7N9. These 'new' respiratory viruses are potential threats to the immune system and healthcare systems worldwide ⁽⁷⁾.

Since discovery of the antiviral action of Echinacea in typical common cold viruses, interest has shifted to the activity of the herb against highly pathogenic respiratory viruses. This field of research can only be handled by a few laboratories across the world with the highest bio-safety standards ⁽⁸⁾.

Antiviral spectrum

The antiviral spectrum of Echinaforce® extract has been shown to be broad, with activity against rhinovirus, respiratory syncytial virus, influenza A & B, and their subgroups (H3N2, H5N1, H7N7, H1N1pdm09), and herpes simplex viruses ⁽⁹⁾. Today, new evidence exists that in addition, parainfluenza, coronavirus (229E) and avian influenza virus H7N9 can be inhibited by low concentrations of Echinaforce® extract *in vitro*.

In 2013, the antiviral activity was found to be localised in the leaves of *Echinacea purpurea*. However, the activity was dependent on the extraction method used. Only extracts manufactured from freshly harvested plant parts growing above ground yielded full inhibitory activity. When extracts were produced using dried Echinacea herb, 90% of the antiviral activity was lost ⁽¹⁰⁾.

Pathological effects on airways

Early and effective inhibition of influenza viruses during the initial phase of an infection is particularly important as these pathogens have the potential to produce massive histological changes to airway epithelia.

This tissue disruption can be simulated *in vitro* using organotypic 3D tissue models after infection with H3N2 viruses (Figure 2, left). Echinaforce® extract was found to potently inhibit these pathological effects by preventing excessive extracellular matrix degradation (Figure 2, right).

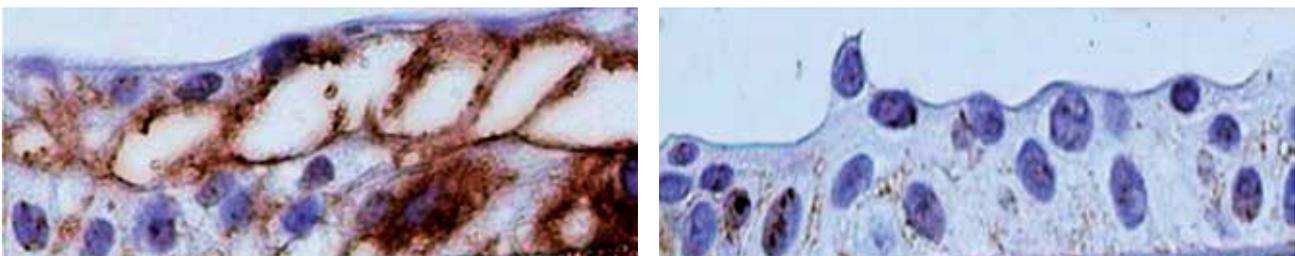


Figure 2: Immunohistostaining of matrix metalloproteinase protein 9 (MMP-9) shows a massive histological disorder of airway epithelia after influenza infection without (left) but not with Echinaforce® treatment (right).

Conclusion

Echinacea extracts have been shown to possess strong and broad antiviral activity against common cold viruses as well as newly emerging, highly pathogenic respiratory viruses. We were able to demonstrate histologically that Echinacea has a protective effect on airway epithelia by preventing extracellular matrix degradation which clinically, increases the risk of complications. These effects were dependent on the method of extraction and crucially, the use of fresh herbs as the starting material.

Prevention of RTI Recurrences and Complications by Echinacea⁽¹¹⁾

Prof. Sebastian L. Johnston, Imperial College London, United Kingdom

Acute viral respiratory tract infections (RTIs) are the most frequent illnesses in Western civilization⁽¹⁾. We know them as mild to moderate forms of the common cold or more severe flu or influenza. Every infection has the potential to deplete immune function and irritate airways epithelia (Figure 1).

This increases the likelihood of recurrent infections and complications which include pneumonia, sinusitis and bronchitis. The incidence of these complications is significant – for instance, studies show that up to 20% of influenza infections lead to complications⁽⁴⁾.

In this study we addressed the question whether Echinacea could positively influence prognosis of RTIs and thereby prevent recurrences of infection and the development of complications.

Data from six clinical studies with a total of 2458 participants were included in the meta-analysis. In five, Echinacea was taken for periods between 2 and 4 months continuously and the 6th employed a protocol of 10 day treatment periods, repeated in response to acute infections over a period of 4 months.

Recurrent Infections

The use of Echinacea was found to significantly prevent the risk of recurrent infections by 35% (relative risk, RR=0.650 (95% confidence interval [CI] 0.545–0.774); p<0.0001). Ethanolic extracts of Echinacea appeared to possess superior effects over pressed juices, and strong effects (reduction by 50%) were seen with continuous long-term prophylactic use over 2 to 4 months.

Individuals with an increased risk of RTIs include those under stress, poor sleepers and smokers, with up to 5 infective episodes observed each cold season. In this population, Echinacea halved the risk of recurrent respiratory infections (RR=0.501 [0.380–0.661]; p<0.0001), as seen in figure 3.

Special attention was paid to virologically confirmed RTIs due to the antiviral potential of Echinaforce[®]⁽⁹⁾. A 58% reduction of viral re-infection was observed in those using Echinaforce[®] extract (RR=0.420 [0.222–0.796]; p<0.0001).

Effect of Echinacea on recurrent RTIs – Subgroups with increased susceptibility

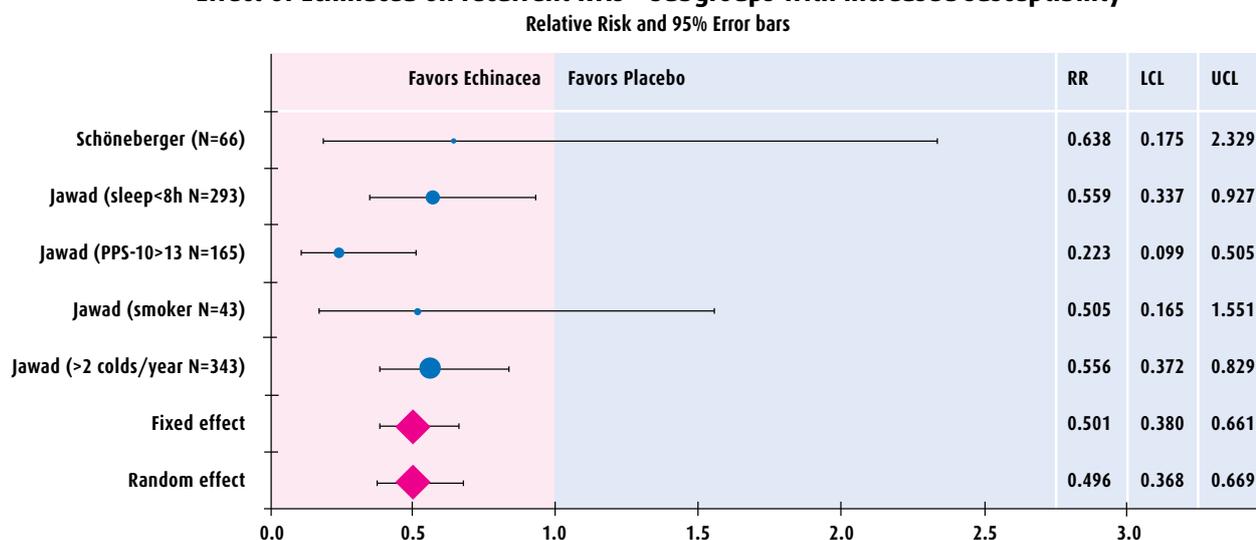


Figure 3: Individuals susceptible to RTIs are an ideal population for studying recurrent infections⁽¹²⁾. Risk reduction (RR) of recurrences in the Echinacea group vs placebo group. LCL and UCL = lower and upper confidence limits.

Complications

Data on complications arising from RTIs was available from 3 prevention trials and meta-analysis showed that complications were significantly higher in the placebo group (Figure 4). This data also suggests that 65% of cases with pneumonia could be prevented by taking Echinacea (RR=0.351, $p<0.0001$) and the overall risk of developing a complication was reduced by approximately 50% ($p<0.0001$).

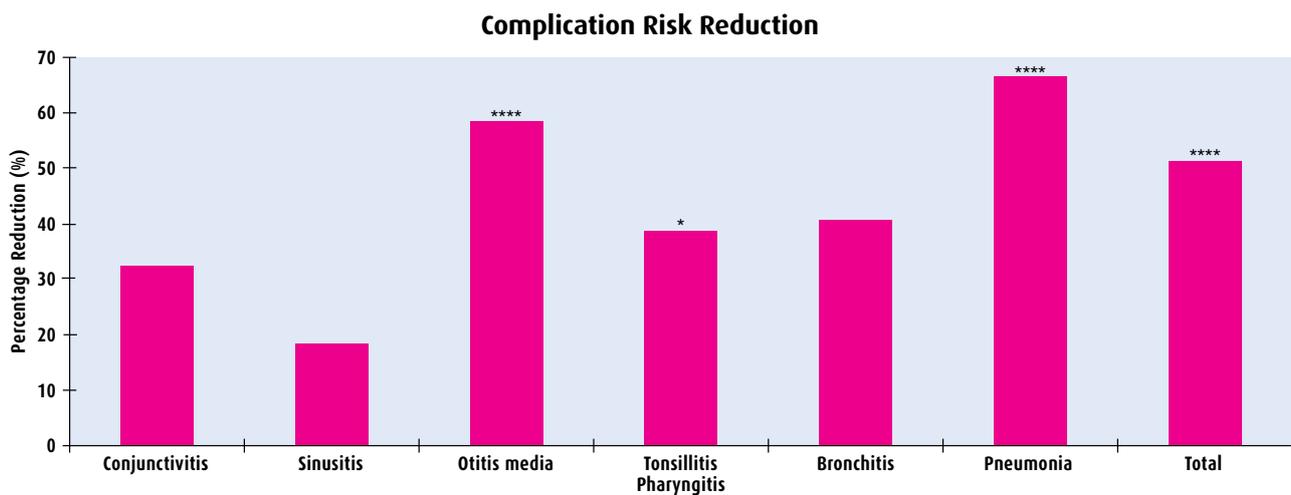


Figure 4: Use of Echinacea extracts was associated with a significant reduction in total complications. Most prominent effect was seen in the incidence of pneumonia. * $p<0.05$; **** $p<0.0001$.

Conclusion

RTI complications such as pneumonia, sinusitis or bronchitis are major clinical issues with a high number of hospitalisations, significant morbidity and mortality ⁽⁷⁾. To date, no medicinal treatment has been shown to prevent unfavourable progression of RTIs, recurrences and the consequent risk of complications.

This is the first time we have evidence that Echinacea not only prevents recurring RTIs but also the complications arising out of these infections. Echinacea appears to positively influence progression of colds and flu. Strongest effects were seen with continuous use of ethanolic extracts over a period of 2 to 4 months, with the risk of developing pneumonia reducing by 65%.

Echinaforce® Hot Drink versus Oseltamivir in Treatment of Influenza⁽¹³⁾

Dr. Peter Fisher, Royal London Hospital for Integrated Medicine, United Kingdom

With its ability to produce epidemics and pandemics, severe illness and the enormous pressure to the Western healthcare system, infection by influenza viruses presents a special case in the management of RTIs⁽¹⁴⁾.

Neuraminidase inhibitors such as Oseltamivir are today recommended for the treatment of the early stages of influenza. This class of drugs block the release of newly produced virions⁽¹⁵⁾.

Echinaforce®, on the other hand, is understood to inhibit infectivity of the progenitor virus⁽⁸⁾. Despite different modes of action, both block viral dissemination and the development of illness.

In this large clinical trial, 473 patients with clinically diagnosed influenza were allocated to treatment with either Echinaforce® Hot Drink (over 10 days) or Oseltamivir (over 5 days followed by 5 days placebo). Nasal secretions were collected at first visit to help define the period of highest influenzal activity.

Recovery from illness

Figure 5 shows the percentage of recovered patients per treatment day in both groups. Very similar rates of recovery were observed with Echinaforce® Hot Drink and Oseltamivir. The efficacy of Echinaforce® was seen in those diagnosed with influenza clinically, during peaks of influenza infection, as well as in those with virologically confirmed infections.

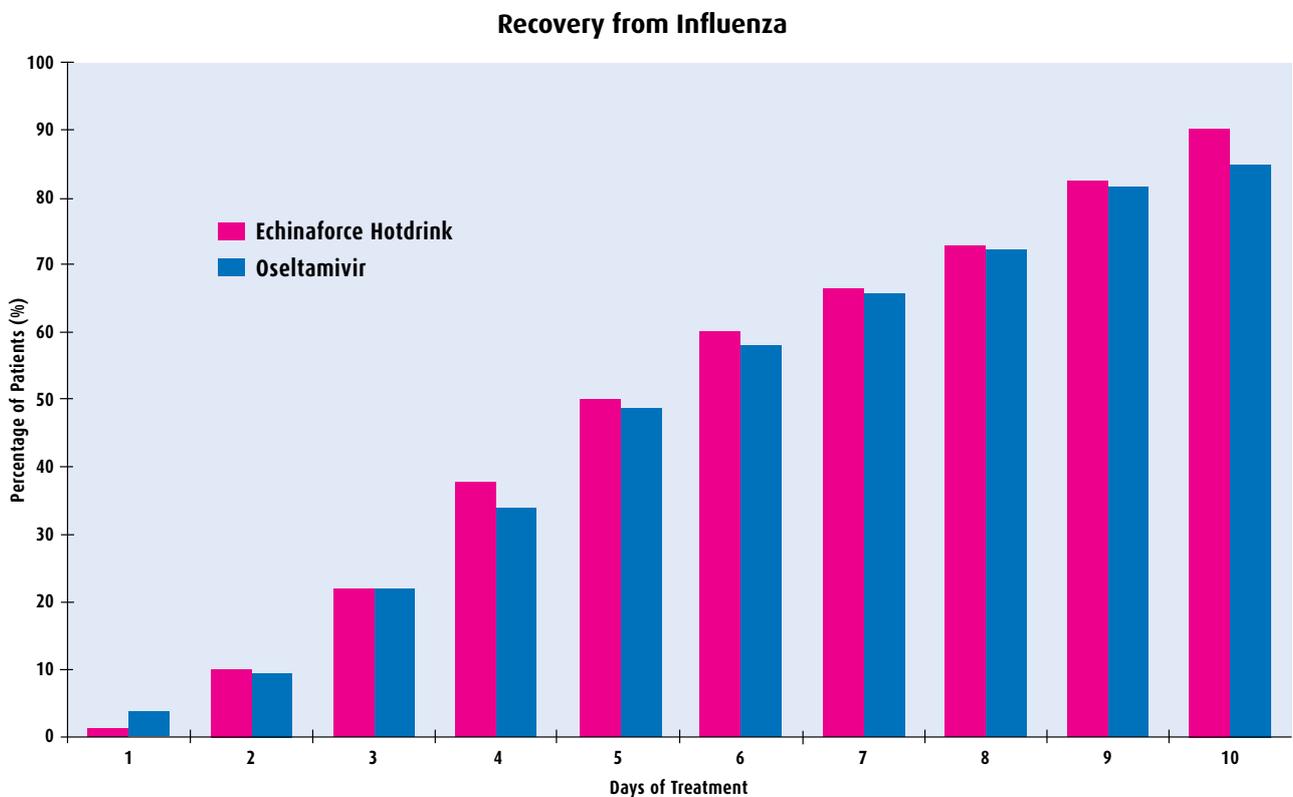


Figure 5: Proportion of patients with symptom resolution per treatment day

Complications

The incidence of complications was also measured. In the Oseltamivir group, pneumonia, sinusitis, bronchitis and other complications occurred at a rate of 6.5% compared to 2.5% in the Echinaforce® Hot Drink group (Figure 6).

In 91.6% of cases, investigators considered the efficacy of Echinaforce® Hot Drink to be “good” or “very good”.

Gastrointestinal complaints leading to the premature interruption of treatment were observed with Oseltamivir but not Echinaforce®. Adverse events were reported by 26 patients using Echinaforce® (11.4%) and 32 patients taking Oseltamivir (13.9%). 15 reports of nausea and vomiting were recorded in those using Oseltamivir in comparison to 3 reports with Echinaforce® Hot Drink. No patient required hospitalisation and no severe adverse event was observed.

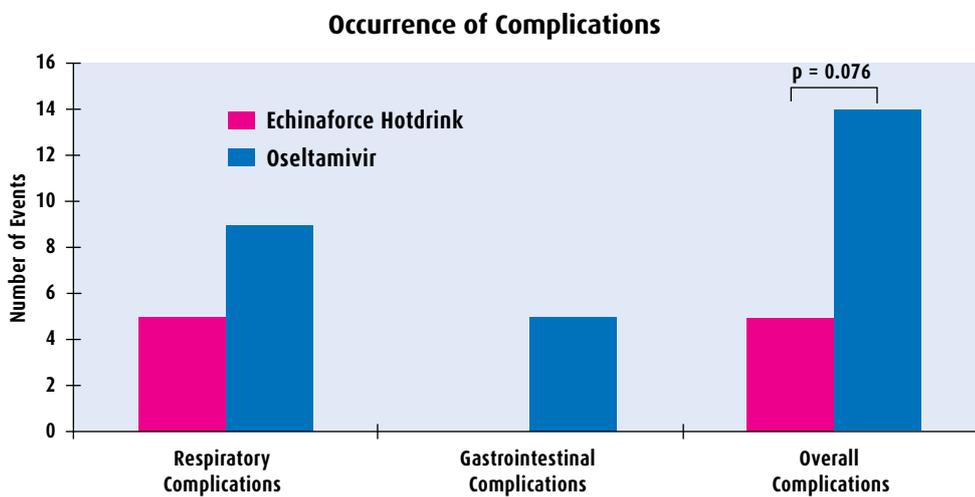


Figure 6: Occurrence of complications under Echinaforce® Hot Drink and Oseltamivir treatment.

Conclusion

In this study, Echinaforce® Hot Drink was shown to be as effective as the neuraminidase inhibitor Oseltamivir, the gold standard for treatment and prevention of influenza.

The clinical efficacy of Echinaforce® was seen in those diagnosed with influenza clinically, during peaks of influenza infection, as well as in those with virologically confirmed infections.

Echinaforce® Hot Drink outperformed Oseltamivir in measures of risk of complications and safety. Unlike Oseltamivir, its availability as an over-the-counter medicine makes it appropriate for the treatment of influenza at the earliest onset of symptoms, an essential factor in the effective treatment of this common viral infection.

Echinacea – New Therapeutic Options

Dr. Andreas Schapowal, ENT Specialist, Landquart, Switzerland

Today's therapeutic arsenal has no effective option for the prevention of complications arising as a result of the respiratory tract infections we know as the common cold or 'flu.

From a clinical point of view, such a therapeutic agent would be highly useful as the consequences of single episodes of colds or flu can be substantial if sequelae such as pneumonia, sinusitis or bronchitis arise. Despite the well-known effects of the overuse of antibiotics on bacterial resistance, many physicians fall back on antibiotics, often as a response to patient pressure, when faced with these conditions.

On the other hand, many patients rely on self-medication with proprietary medicines containing paracetamol and ibuprofen for immediate symptom relief when treating colds and flu. However, latest research indicates that these pharmaceuticals may further increase the risk of complications and the need for a second consultation⁽⁶⁾.

These analgesic medicines have no impact on the infecting virus and no activity in supporting the action of the immune system – two central factors to consider when treating RTIs.

The novel insights seen recently with Echinacea underline the importance of this medicinal plant in the management of RTI.

Data from previous studies indicated that Echinacea can prevent colds and alleviate acute symptoms of infection⁽¹⁶⁾. We have now seen that, in addition to these primary actions, the effects of Echinacea include reduction in the risk of recurrent infections and complications.



The effects are however, dependent on the type of extract used. For instance, the broad antiviral activity of the medicinal plant is only found in the parts of the herb growing above ground and, if freshly harvested herbs are used as the starting material.

Fresh Echinacea extracts containing both the herb and root have a wide antiviral potential and also support function of the immune system⁽¹⁷⁾. This leads to several important implications for the use of Echinaforce® in the management of RTIs:

 <p>PREVENTION</p>	<ul style="list-style-type: none"> New! • Of initial and recurrent infections New! • Of pneumonia or bronchitis • In those with weak immune function – those under stress and smokers benefit most
 <p>ACUTE THERAPY</p>	<ul style="list-style-type: none"> • Reduction in duration and severity of RTI New! • Co-therapy with paracetamol / ibuprofen New! • Safe and effective influenza treatment New! • Prevention of complications

Clinician's Insider Tips:



- Start treatment at occurrence of first symptoms
- Increase dosage during first 2 – 3 days
- Continue treatment throughout the time of convalescence
- If you use paracetamol and ibuprofen then use Echinacea alongside
- Susceptible individuals to use Echinacea for long-term treatment
- Use products manufactured from freshly harvested *Echinacea purpurea*

Expert Panel



Prof. Sebastian L. Johnston

National Heart and Lung Institute. Imperial College London (United Kingdom)

Sebastian Johnston is Professor of Respiratory Medicine & Allergy at the National Heart and Lung Institute, Imperial College London and Honorary Consultant Physician in Respiratory Medicine & Allergy at St Mary's Hospital, Imperial Healthcare NHS Trust, London. He is an expert in the field of respiratory tract infections and therapeutic interventions. He contributed to the modern understanding of respiratory infections and their medicinal consequences (e.g. asthma exacerbations).



Dr. Peter Fisher

Royal London Hospital for Integrated Medicine (United Kingdom)

Peter Fisher is Director of Research at the Royal London Hospital for Integrated Medicine (RLHIM), part of the University College London Hospitals NHS Foundation Trust. He is also Physician to Her Majesty Queen Elizabeth II. He is a member of the Expert Reference panel of the UK National Institute of Health and Care Excellence (NICE). Peter Fisher's research work centres on responding to the problems in health care, including 'effectiveness gaps', multimorbidity and polypharmacy, by integrating the best of traditional and complementary medicine.



Dr. Oliver Engler

Federal Office for Civil Protection, Spiez Laboratory (Switzerland)

Oliver Engler is researcher and Deputy Head of the Virology Department of the Laboratory in Spiez, Switzerland. The Virology group specialises in the detection of human pathogenic viruses of the biosafety levels 2, 3 and 4, which can be used as biological warfare agents and/or are of epidemiological significance for the national civil protection.



Dr. Selvarani Vimalanathan

Immunity and Infection Research Center, University of British Columbia (Canada)

Selvarani Vimalanathan is a researcher at the Immunity and Infection Research Centre, University of British Columbia. She has wide experience with respiratory viruses such as influenza and studies their interaction with the human airways epithelia. She has also worked on the interaction of viruses with cells of the immune system.



Dr. Andreas Schapowal

ENT Specialist, Landquart (Switzerland)

Andreas Schapowal MD, PhD, DSc (hon) is a specialist in oto-rhino-laryngology, allergies and clinical immunology, psychosomatic and psychosocial medicine. As former head of the ENT Department in Davos, medical consultant to the World Economic Forum, lecturer to Hannover Medical College and from the many years in his own practice, he has very extensive experience in treating colds and flu.



Prof. Michael Heinrich

Centre for Pharmacognosy and Phytotherapy, UCL School of Pharmacy, University of London (UK)

The conference will be chaired by Professor Michael Heinrich, Head of Centre for Pharmacognosy and Phytotherapy at the School of Pharmacy (University London). His expertise covers the areas of pharmacognosy, phytochemistry, ethnopharmacology and ethnopharmacy. Recent research explored value chains of herbal medicines, the safety of herbal medical products and the use of medicinal plants in immigrant communities.

References

1. Fendrick AM, Monto AS, Nightengale B, Sarnes M. The economic burden of non-influenza-related viral respiratory tract infection in the United States. *Arch Intern Med.* 2003; 163: 487–94.
2. Aherne W, Bird T, Court SDM, Gardner PS, McQuillin J. Pathological changes in virus infections of the lower respiratory tract in children. *J Clin Pathol.* 1970; 23: 7–18.
3. Message SD, Johnston SL. Host defense function of the airway epithelium in health and disease: clinical background. *J Leukoc Biol.* 2004; 75: 5–17.
4. Kaiser L, Wat C, Mills T. Impact of oseltamivir treatment on influenza-related lower respiratory tract complications and hospitalizations. *Arch Intern Med* 2003;163:1667-1672.
5. Kenealy TW, Arroll B. "Antibiotic use for common cold", in *Common Cold*, Eccles RWO, Ed. (2009) pp 132 – 133, Birkhäuser Verlag, Basel, Switzerland.
6. Little P, Moore M, Williamson I, Leydon G, McDermott L, Mullee M, Stuart B. Ibuprofen, paracetamol and steam for patients with respiratory tract infections in primary care: pragmatic randomized factorial trial. *BMJ.* 2013;347:1-13.
7. Fleming DM, Elliot AJ, Nguyen-van TJS, Watson JM, Wise R. *A winter's tale: Coming to terms with winter respiratory illnesses.* Health Protection Agency, London. 2005.
8. 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). *Viol J.* 2009; 6: 197.
9. 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;83:165-170.
10. Vimalanathan S, Schoop R, Hudson JB. High-potency anti-influenza therapy by a combination of Echinacea purpurea fresh herb and root tinctures. *JAPS*;3(12):1-5.
11. Schapowal A, Klein P, Johnston SL. Echinacea reduces the risk of recurrent respiratory tract infections and complications: a meta-analysis of randomized controlled trials. *Adv Ther.* 2015;32(2):187-200.
12. Jawad M, Schoop R, Suter A, Klein P, Eccles R. Safety and efficacy profile of Echinacea purpurea to prevent common cold episodes: a randomized, double-blind, placebo-controlled trial. *ECAM.* 2012; 2012: 841315. doi: 10.1155/2012/841315.
13. Raus K, Schoop R, Pleschka S, Klein P, Fisher P. Echinaforce Hotdrink versus Oseltamivir in influenza: A randomized, double-blind, double-dummy, multicenter, non-inferiority clinical trial. *Curr Ther Res* 2015; accepted for publication.
14. Thompson WW, Shay DK, Weintraub E, et al. Mortality associated with influenza and respiratory syncytial virus in the United States. *JAMA.* 2003;289:179-186.
15. Bardsley-Elliot A, Noble S. Oseltamivir. *Drugs* 1999;58:851-60.
16. Shah SA, Sander S, White CM, Rinaldi M, Coleman CI. Evaluation of echinacea for the prevention and treatment of the common cold: a meta-analysis. *Lancet Infect Dis.* 2007; 7: 473–80.
17. Ritchie MR, Gertsch J, Klein P, Schoop R. Effects of Echinaforce® treatment on ex vivo-stimulated blood cells. *Phytomedicine* 2011; 18: 826–831.



Bioforce AG
9325 Roggwil
Switzerland
info@bioforce.ch
www.avogel.com

Echinaforce®

- ✓ Extract of freshly harvested *Echinacea purpurea*
- ✓ Combination of 95% herba and 5% radix
- ✓ Standardised ethanolic extract
- ✓ Grown from own (recycled) seeds
- ✓ Organically (biologically) cultivated

