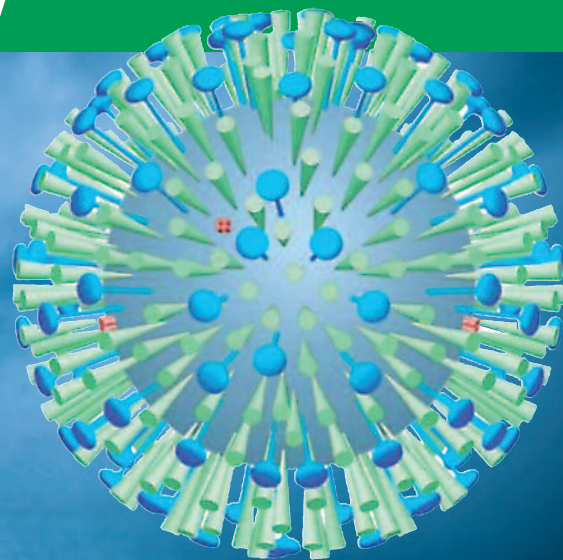


FOR EXPERTS IN HEALTH CARE

Important innovations in phytotherapy

# Echinaforce<sup>®</sup>, antiviral, antibacterial and antiinflammatory



*A.Vogel*

## Introduction

The wide acceptance of medicinal plants in the population is reflected in an increase in research activity and in the continuing and strongly rising number of scientific publications on phytotherapy (doubling within the past 10 years).

These have revealed new properties and potentials especially in such well-known medicinal plants as the purple coneflower (*Echinacea purpurea* (Latin) Moench).

Recently, researchers at the Justus-Liebig University of Giessen in Germany and the University of British Columbia in Vancouver, Canada, have provided particularly impressive examples. They demonstrated that a specific fresh plant extract of Echinacea (Echinaforce®) not only has marked antiviral effects but can also normalises the immune system's pathological overreactions in viral infections.

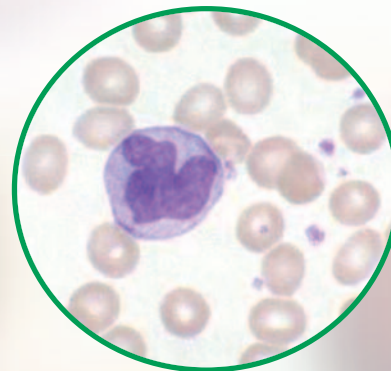
This not only explains why Echinacea is effective both in acute treatment and in prophylaxis; it also opens up the prospects of new medical applications.

## The enigma of Echinacea therapy

In the classical understanding, the basis for using preparations of purple coneflower to prevent infection is that once Echinacea is taken it supports the body's immune system (non-specific systemic immune stimulation) – for example, the multiplication and enhanced activation of immune cells or the consequent optimisation of humoral immune responses.

These systemic effects might also explain the demonstrable therapeutic effects on the course of colds and influenza like infections when used at a very early stage.

The essential difficulty with this pharmacodynamic theory is that the strengthening of non-specific endogenous immunity takes time, several days at least – as do many of the body's immune reactions. The theory can therefore not explain why Echinacea extracts are also so rapidly effective in acute treatment.



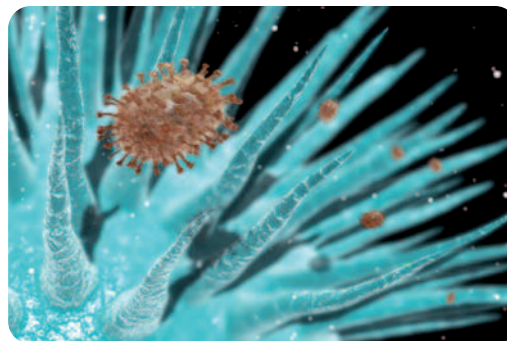
*Echinacea is reported to support the immune system via the activation of lymphocytes and macrophages.*

# Antiviral effects of Echinaforce®

Anti-viral

Over the past decades, scientists have repeatedly speculated that Echinacea extracts might have direct antiviral effects, for instance on herpes simplex viruses. The latest research findings now show that a special extract (Echinaforce®) does indeed have broad antiviral effects on relevant pathogens of upper respiratory tract infections, in a standard infection model [1].

The antiviral effects were explored in a cell culture infection model, in which cells from the human respiratory tract (including bronchi and alveoli) were treated with Echinaforce® and infected with various pathogenic viruses. The objective was to determine the smallest dose of Echinacea which completely inhibited viral multiplication.



The results were absolutely unequivocal. Even the smallest amounts of Echinaforce® completely inactivated influenza and herpes simplex viruses, and also respiratory syncytial viruses. Higher concentrations were needed for other common pathogens of colds, such as rhinoviruses or adenoviruses.

Antiviral activity		MIC100 (µg/ml)
Enveloped viruses	Influenza (A/H3N2, human), flu	0.58±0.22
	Herpes simplex (HSV, type 1), herpes labialis, and any others	0.39
	Respiratory syncytial virus (RSV), upper-respiratory tract infections especially in infants and children	2.50
Non-enveloped viruses	Rhinovirus (types RV1A and RV14), colds, bronchitis	>800
	Adenovirus (types 3 and 11), respiratory tract infections	>800
	Feline calicivirus (FCV), cat flu	>800

MHK<sub>100</sub> – lowest concentration of a substance that completely inhibits viral multiplication. In this case, therefore, the lowest concentration of Echinacea extract, in µg/ml, necessary for complete viral inactivation.

# Has Echinaforce® any effect on new influenza viruses?



Based on the antiviral activity of Echinaforce® against different common respiratory tract viruses (see page 3) an international team of researchers

explored whether Echinaforce® would offer a complementary option for the treatment of novel types of influenza viruses as well [2].

## The following viruses were examined

Virus types	Virus strains	Pandemic Influenza
A/H3N2	A/Victoria/3/75	z.B. „Victoria“ or seasonal influenza
A/H5N1	A/Thailand/KAN-1/2004	z.B. avian influenza, human pathogenic
A/H7N7	A/FPV/Bratislava/79	z.B. avian influenza, human pathogenic
A/H1N1	A/Hamburg/1/09	Current pandemic influenza called Swine flu or Mexican flu

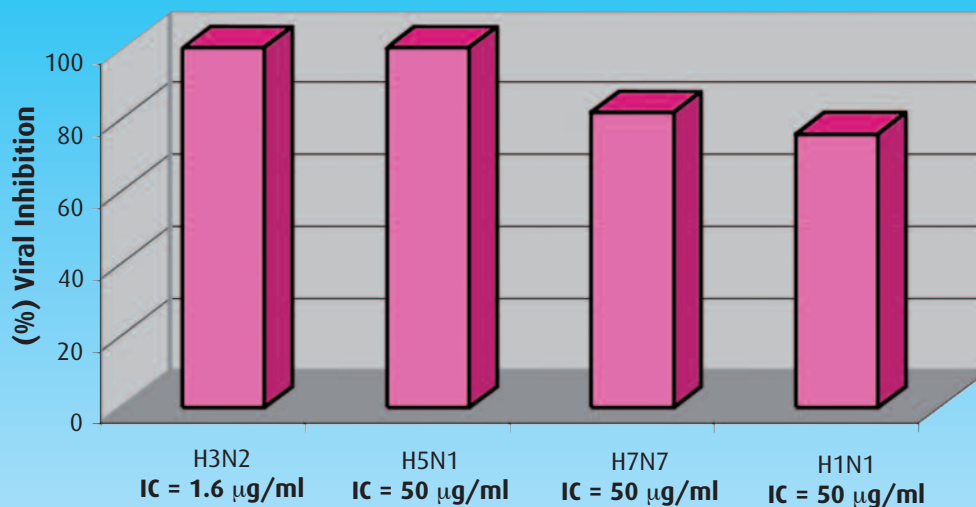
## The researchers have used an *in vitro* infection model

- 1** Epithelial cells were cultured in test-tubes to a confluent layer.
- 2** Cells and/or viruses were treated with Echinaforce® at different times and at different concentrations.
- 3** Cells were infected with the above viruses.
- 4** Formation of lesions (“foci”) in the celllayer showed viral infections → viral activity.
- 5** Reduced numbers of foci indicated the antiviral activity of Echinaforce®.

# Echinaforce<sup>®</sup> against H3N2, H5N1, H7N7, H1N1 – *in vitro*

Anti-  
viral

## Echinaforce<sup>®</sup> inhibits various influenza viruses



- Echinaforce<sup>®</sup> inhibits infectiousness of all influenza viruses significantly
- The needed IC (=inhibitory concentration) was between 1.6 µg/ml to 50 µg/ml
- The IC is far below the local concentrations reached with oral treatment
- The effect remained unchanged even with high virus load (e.g. 10<sup>5</sup> PFU/ml)

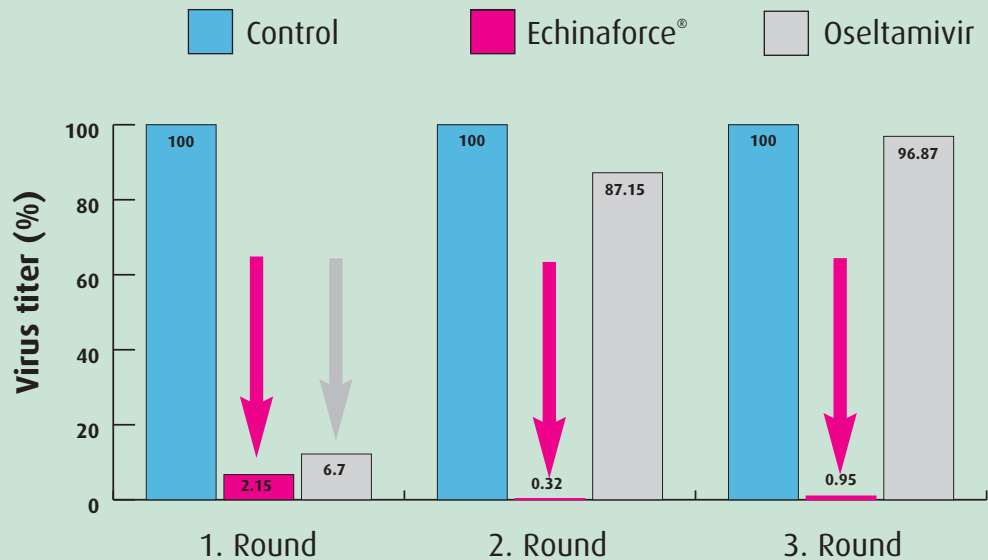
# Echinaforce® does not rise resistances

Anti-viral

Synthetic neuraminidase inhibitors are reported to induce resistances/insensitivity of the

virus towards the treatment in vivo and in vitro. Is this the case with Echinaforce® as well?

## Persistence of efficacy over treatment cycles



- 🌀 Echinaforce® constantly inhibits viruses over several rounds of treatment.
- 🌀 With Echinaforce® no resistant virus strains emerged not even after several rounds of treatment cycles.
- 🌀 Repeated treatments with oseltamivir evokes resistant viruses: 87% of viruses were resistant at the 2nd, 97% at the 3rd cycle.
- 🌀 Echinaforce® even blocks viruses, which are resistant to oseltamivir treatment.

# Molecular mechanism; Echinaforce® inhibits the virus adhesion



The particularly challenging scientific question concerns the molecular mechanism of these antiviral effects. The analyses conducted by the group of researchers show that contact between the viruses and the Echinacea extract leads to the inhibition of infectiousness early on during the infection process. The reason for this is that the

viral surface protein haemagglutinin (HA) is modified in such a way that it is no longer able to dock onto body cells. If this important stage of the infection cascade is stopped, the influenza viruses are no longer able to penetrate into the cells and replicate.

- **Echinaforce® blocks viruses at the earliest step in the infection process.**
- **Echinaforce® modifies the viral surface protein hemagglutinin, which is essential for viral infection.**
- **Consequently, viral adhesion to cell receptors is interrupted.**
- **The influenza viruses can no longer penetrate into and replicate inside cells.**

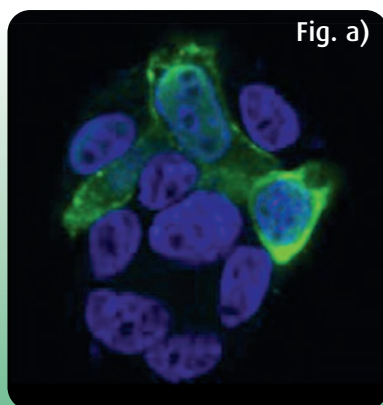


Fig. a)

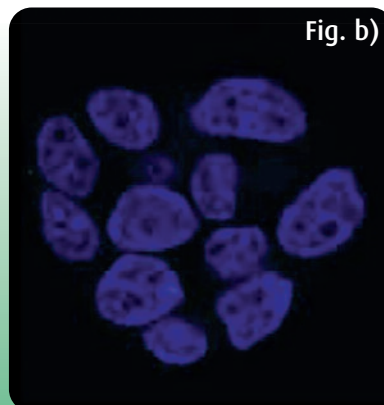


Fig. b)

Figure a)  
The histological staining of the influenza replication factor (green) shows how untreated viruses infect epithelial cells (blue cellular nucleus).

Figure b)  
Echinaforce® blocks the viral docking-receptors and prevents infection.

# Antibacterial effects of Echinaforce®

Anti-bacterial

Echinacea has an extensive history of effective use in both internal and external bacterial infections. The native North-Americans and later the eclectic US-herbalists used extracts from this plant long before the availability of modern antibiotics. Recent studies evaluated the direct antibacterial effects of the well-known echinacea fresh plant extract Echinaforce® [3]. The bactericidal (bacteria killing) effect was tested with several bacterial pathogens, which are important for acute respiratory tract infections and exacerbation.

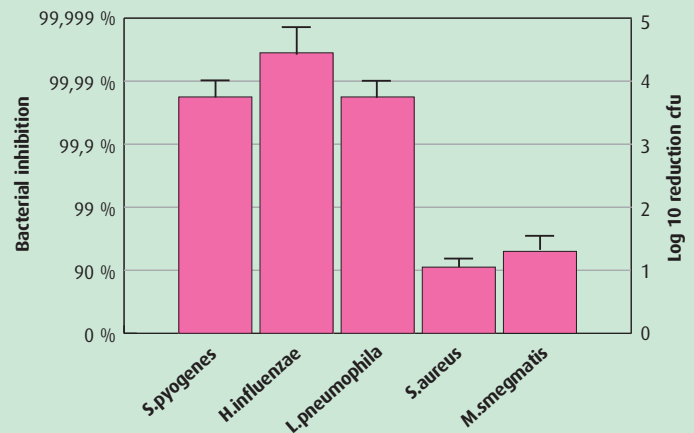
The results confirmed the traditional and empiric knowledge: Echinacea in fact has bactericidal effects on important pathogenic bacteria like

*Streptococcus pyogenes*, *Haemophilus influenzae* or *Legionella pneumophila*. These microbes were completely deactivated by echinacea (by 99.90–99.99%) in low concentrations (<160 µg/ml dry mass). Other bacteria like *Staphylococcus aureus* needed higher extract dilutions for the bactericidal effect.

In the many cases of bacterial superinfection of originally viral respiratory tract infections (the so called “bacterial exacerbation”), this antibacterial effect of echinacea can improve considerably the therapeutic management. Thus Echinaforce® might deliver a preventive effect against the development of pneumonia, sinusitis or bronchitis.



Antibacterial activity of Echinaforce®



Incubation of the bacteria (concentration of  $\sim 6 \times 10^8$  cfu (colony forming units)/ml) with Echinaforce® (dilution of 1:100) and the bacterial inactivation in percentages and in a log range [1].

# Clinical importance of the anti-microbial effects of Echinaforce®

Every direct antiviral and antibacterial effect of a medicinal product potentially reduces:

- **first**, the extent of the primary infection; and
- **second**, the topical spread of the agent, for example in the lower airways.

Mainly with completely unknown viruses the body's response is often inadequate and in this context the minimization of the viral load can help the organism to manage the infection.

The nasopharyngeal space is the tissue to be first infected by many respiratory viruses and therefore represents a bottleneck for further dissemination also to the airways. Sucking Echinaforce® tablets or using Echinaforce® Sore Throat spray effects a strong antiviral protection in the pharyngeal space. Thereby the local concentration of Echinaforce® is much higher than the smallest effective dosage in the experiments.



high microbial load



a reduced microbial load improves management of infections

“Virology Journal publication”  
**conclusion by the authors**

*Echinaforce® has the potential to impair influenza virus propagation (H3N2, H5N1, N7N7, H1N1) at concentrations recommended for oral use and below. This potential, the availability and the lack of toxicity make this preparation an interesting option in the control and treatment of influenza virus infection.*

# Echinaforce® in infectious cytokine storms



Anti-inflammatory

A considerable part of the symptoms of a flu-like infection is caused not by the viruses or bacteria themselves but by the reactions of the organism to pathogens.

Therefore, the immune system, in its efforts to rid itself of the micro-organisms, can harm the body's own cells and produce symptoms.

An unbridled overreaction of the immune system ("cytokine storm") can even explain why certain influenza viruses are especially dangerous, as was recently apparent in bird flu sufferers, and also during the Spanish flu.

Two newly published in vitro studies [1, 4] deal with the secretion of proinflammatory cytokines in the mucosal cells of the respiratory tract after viral infection. They investigate whether Echinaforce® could have a beneficial effect on pathological processes of this kind.

Cell cultures were infected with different viruses, mainly pathogens of upper respiratory tract infections. Echinaforce® was used for treatment in varying amounts and at different times.

The main target was the concentration of proinflammatory signal proteins, which the cells secrete into the culture medium in increased amounts after viral contact.



# Echinaforce® in infectious cytokine storms

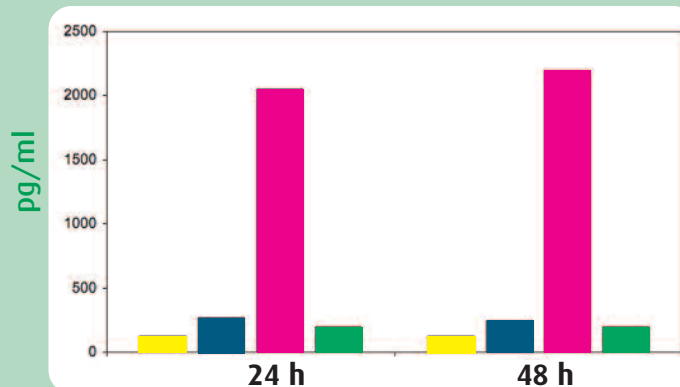
Anti-inflammatory

The studies tested human influenza viruses and also various types of herpes simplex, rhinoviruses, adenoviruses and respiratory syncytial viruses. They showed that Echinaforce® blocked the release of all inflammatory mediators studied (including interleukin-6, interleukin-8 and TNF- $\alpha$ ) after virus infection. These anti-inflammatory activities of the preparation were apparent in all tested respiratory viruses [4].

It was shown that infection with rhinoviruses provoked proinflammatory cytokines interleukin-6 and interleukin-8 after only four hours. Previous or subsequent treatment of the cells with Echinaforce® almost completely prevented this reaction.

The cytokine release was also blocked if Echinaforce® was not added until 48 hours after infection. The effect of Echinaforce® was dose-dependent and time-related, and was clearly evident at even the lowest doses, and already after 30 minutes of exposure.

Interestingly bacteria elicit the inflammation in similar ways as viruses do although other mediators are involved (like IL-8 MCP-1, 1 GM-CSF). Echinaforce® prevented the production of inflammatory mediators, even if these were induced by bacteria [3].



Secretion of interleukin-8 from human bronchial cells 24 and 48 hours after the start of the test.

- Control system with untreated cells
- Control culture after addition of Echinaforce®
- Infection with rhinoviruses (⇒massive increase)
- Infection plus Echinaforce® (⇒normalization of cytokine secretion)

# Importance of the anti-inflammatory effect provided by Echinaforce®

Anti-inflammatory

The over-reaction of parts of the immune functions plays an important part in the pathogenesis of many diseases.

The over-reaction is often disproportionate to a trivial infection e.g. with rhinoviruses.

The understanding of the pathogenesis is fundamentally altered by the fact that an uncontrolled and excessive secretion of proinflammatory signal proteins, can evoke symptoms of influenza infections.

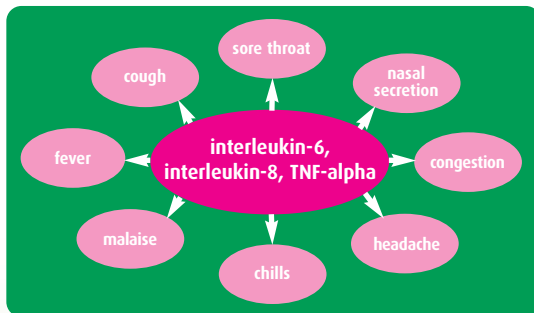
It is often not the pathogens themselves but the body's conflict with them, which causes the pathological symptoms. The fact that Echinaforce® is also involved here explains why it is effective

even when an infection has already broken out, i.e. in acute therapy.

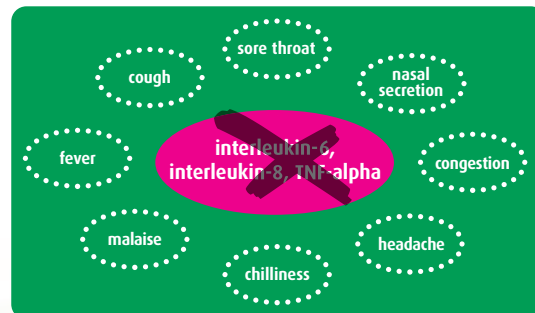
On the other hand, the regulation of excessive reactions of the immune system caused by Echinaforce® provides the organism with an effective aid to self-healing.

Ultimately, the subjective alleviation of symptoms is a strong argument for many users, in view of the often highly unpleasant and troublesome symptoms.

*Echinaforce® inhibits the symptoms of infection by blocking proinflammatory signal proteins. (as shown in-vitro)*



untreated



treated

Echinacea normalizes the excessive release of proinflammatory cytokines by respiratory cells as induced by both viruses or bacteria.

# Questions and answers

Is Echinaforce an herbal antimicrobial substance, comparable to virustatics or antibiotics? Are we still talking about natural medicine?

*The different antimicrobial components in the fresh plant echinacea extract actually reduce the infection rate of cells from viruses and consequently the viral load. The new in vitro studies demonstrate clearly that Echinaforce® directly inhibits various respiratory viruses, comparable to modern virustatics. Probably by modifications of the virus surface which block cellular infection. In addition Echinaforce® has some bactericidal, i.e. bacteria killing effects like typical antibiotic compounds. It is important to note that both antimicrobial activities do not alter the body's fundamental tasks of dealing with the infection.*

*Natural medicine often uses mechanisms that are also employed by conventional mechanisms without being designated as such. If direct elimination of the microorganisms and enhancement of the body's own endogenous healing powers complement one another, we are speaking about modern evidence-based phytotherapy. It should also be noted that antimicrobial mechanisms are essential abilities of all living creatures (e.g. antibiotics are predominantly derived from natural sources like the Penicillium-fungi). Therefore, Echinaforce® accomplishes both a rational and a natural way of infection control.*

Is it known which ingredients of Echinaforce® constitute the antiviral, antibacterial or immune-modulating effect? Would it not be worthwhile to isolate these and then use them at high doses?

*Antiviral and immune-modulating substances are different from each other. Switching to the isolated single substances would narrow the spectrum of action and probably also increase resistances, undesirable effects and medical interactions as seen with chemical components.*

Can these findings about Echinaforce® be extrapolated to other extracts?

*They can not be extrapolated, first, because this composition of Echinaforce® is unique in the world (95% Echinacea plant, 5% Echinacea root). Secondly, because there are considerable differences in the composition of the extracts, depending on the source of the raw ingredients, and especially on the pharmaceutical processing. This is one of the reasons why Echinaforce® is constantly tested for uniform product quality. More exhaustive studies with extracts produced differently from Echinaforce® show that most of the antiviral effect is lost. The immune-modulating effects are also non-transferable.*



# Questions and answers

**?** If Echinaforce® is so effective for acute treatment, is there any point in using it long-term?

*The acute treatment of respiratory tract infections is definitely indicated whenever the first signs of such infections are noticed, including malaise, limb pain, sore throat or the onset of catarrh. The earlier the Echinaforce® treatment is given, the better are the prospects of alleviation.*

*Prophylactic use is sensible when infections are prevalent, so that endogenous resistance can be built up in a timely manner. So far clinical trials show that the prophylactic protection is fully*

**!** *developed after about 1 to 2 weeks of Echinacea treatment. As we never know exactly when the infection will strike, it can make sense to start prevention early.*

*Many influences (nutrition, stress, disturbed bio-rhythms, etc.) can weaken the functions of the immune system. Signs of a weakened immune system, such as chronic tiredness, recurrent infections, herpes outbreaks or poor wound healing should be recognised as indicators to start using Echinaforce®. In case of long-term use, short intermediate pauses of 5–7 days are recommended.*

## GLOSSARY

<b>Acute therapy</b>	Treatment of an illness during the acute phase
<b>Immune system</b>	Organs, tissues, cells and their functions, which are intended to ensure that the body is not harmed during interaction with the internal and external environment.
<b>Chronification</b>	Beside healing or death, the third potential course of an infection.
<b>Self-help aid</b>	Healing is always achieved by the organism itself. External influences can act to help/support or inhibit/block this process.
<b>Immune modulation</b>	Using medicinal products to influence the functions of the immune system to modulate immune response. This can mean to strengthening these functions (stimulation), blocking them (suppression), or normalising them (harmonisation).
<b>Resistance/insensitivity</b>	The resistance of an organism to external influences (e.g. to a medication or therapy).
<b>Natural medicine</b>	The totality of medical procedures which are derived from the knowledge that the maintenance of health and healing is essentially achieved by the organism itself rather than being achieved by the medication (see Self-help aid).
<b>Pharmacodynamics</b>	The science of the effect of drugs in the body.
<b>Phytotherapy</b>	The science of the process of healing on the basis of herbal medicines.
<b>proinflammatory</b>	Promoting or boosting inflammation.
<b>Cytokine</b>	Some of body's signal substances, consisting of proteins and sugars, which regulate the growth, differentiation and functions of the body's cells. In the area of the immune system they are often called mediators.
<b>Cytokine storm/hypercytokinaemia</b>	In infections, excessive secretion of cytokines. Causes symptoms above all in trivial infections.

# Echinaforce® – evidence-based modern phytotherapy

The findings of these present studies show that this traditional medicinal herb **has completely novel effects**, which are an addition to the previously known range of activity. These findings answer some long-unsolved questions, such as how to explain the well-documented prophylactic effect and the acute treatment of an infection.

Echinaforce®'s antiviral activity is also encouraging the acute use of this traditional natural medicine during increased occurrence of threatening infections. It can be used in conjunction with other measures if necessary.

Echinaforce® has a triple mode of action



Anti-  
viral



Anti-  
bacterial



Anti-  
inflam-  
matory

# Advantages of Echinaforce®

Made from organically grown plants

Extracted from fresh herbs

Made with respect and care

Combines 95% herba extract with 5% radix extract

Compelling chain-of-evidence



Pioneer in Natural Health  
– since 1923

*A. Vogel*

## Literature

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[4] Sharma M, Schoop R, Hudson JB: Echinacea as an anti-inflammatory agent: the influence of physiologically relevant parameters. *Phytother Res.* 2009 Jun;23(6):863-7.

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