

New studies on the antiviral effect of *Echinacea purpurea*

Respiratory viruses include not only cold pathogens, but also influenza or coronaviruses. The latter can jump from animals to humans through zoonosis, as was recently the case with the SARS-CoV-2 virus. The vaccines that have since been developed effectively prevent severe disease progression, but the mutability of the virus seems to undermine long-lasting immunity, as vaccine breakthroughs show. Further antiviral preparations are therefore urgently needed that are less susceptible to viral mutations and offer broad protection that is as non-specific as possible. Preclinical data postulated such an effect for *Echinacea purpurea* in 2020, but their transferability to humans was unclear (1). Now further findings on the medicinal plant have become available.

Prevention study in the Covid-19 pandemic

The prevention of viral infections during the Covid-19 pandemic and the spectrum of efficacy of *Echinacea* on different SARS CoV-2 variants were investigated in detail in two research papers.

A first randomised, open-label, controlled clinical trial investigated the potential of *Echinacea purpurea* in the prevention and treatment of viral respiratory infections, particularly SARS-CoV-2 infections (2). The study included 120 healthy volunteers aged 18-75 years. They were randomly assigned to an *Echinacea prevention* or a no-intervention control group. After a run-in week, participants underwent 3 prevention cycles of 2-2-1 months with 2'400mg of *Echinacea purpurea* extract (Echinaforce®, EF) daily. Between each cycle, the therapy was interrupted for one week. Acute respiratory symptoms were treated with 4'000 mg EF for up to 10 days and their severity was recorded in a diary. Nasal/throat swabs and blood samples were routinely taken every month and additionally during acute illnesses. Detection and identification of respiratory viruses,

including SARS-CoV-2, was done by serology and RT-qPCR, which also determined the viral load.

Over the 5-month period, a total of 21 samples tested positive for respiratory viruses under EF prevention compared with 29 samples in the control group, of which 5 and 14 samples were SARS-CoV-2 positive, respectively (RR = 0.37, $p = 0.03$). A total of 10 and 14 symptomatic episodes occurred in the EF and control groups, of which 5 and 8 were Covid-19 illnesses (RR = 0.70, $p > 0.05$). EF treatment of acute episodes significantly reduced the overall viral load by at least 2.12 log, respectively by over 99% ($p < 0.05$).

The time until patients tested virus-negative again was reduced by 8.0 days overall ($p = 0.02$) and by 4.8 days for SARS-CoV-2 ($p > 0.05$) compared to the control group. Finally, EF treatment led to a significant reduction in fever days (11 days compared to 1 day, $p = 0.003$), but not in overall symptomatology, which could be related to unequal co-medication use. There were fewer Covid-19 hospitalisations with *Echinacea*, although the difference was not statistically significant (N = 0 vs. N = 2).

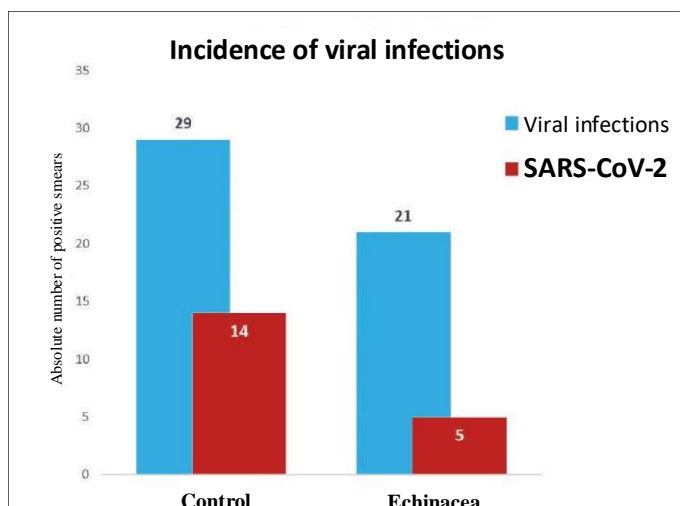
Overall, the study shows a broad antiviral effect of the EF-extract by preventing SARS-CoV-2 as well as other viral infections. The significantly reduced viral load in infected individuals underlines this effect and points to an additional option for prevention and treatment. Although this is a relatively small study, the results are in the context of another new review on the prevention of endemic coronavirus infections by EF extract in adults and children (3).

The above clinical trial was conducted from November 2020 to May 2021, when SARS-CoV-2 alpha, beta and gamma variants were dominant in Europe. As with vaccinations, the question of transferability of results to new variants, such as delta or Omicron, also arises with *Echinacea*. A second paper therefore dealt with the antiviral mechanism of action of *Echinacea purpurea* and the spectrum of action on coronaviruses in general.

Echinacea inhibits endocytosis of SARS-CoV-2

An international team of researchers from 6 universities studied in parallel the effect of *Echinacea purpurea* on SARS-CoV-2 Variants of Concern (VOCs) and on a pseudovirus expressing only the spike receptor. *Echinacea* inactivated all VOCs to about the same extent, namely alpha, beta, gamma, eta or the delta variant were completely inhibited at less than 25 µg/ml Echinaforce® in vitro. The principle of the multi-substance mixture of plant extracts, which could be less susceptible to viral mutations and the emergence of new variants, was suggested as a possible explanation for the broad antiviral protection.

In an earlier publication (Signer et al, 2020), it was criticised that only direct contact with *Echinacea* inactivates the virus,



which could call into question the clinical relevance. A novel approach therefore determined what results the preventive treatment of epithelial cells (without pre-treatment of the virus) would provide: As little as 20 µg/ml EF completely inhibited sequential infection with SARS-CoV-2. Thus, for the first time, a cell-protective effect was demonstrated, which could be central in prevention. Preliminary studies now suggest that EF interacts with TMPRSS-2, a serine protease that is required for the endocytosis of all coronavirus variants to the same extent. This could represent a new, promising approach in the fight against SARS-CoV-2 (4).

Literature:

1. Signer J, et al. In vitro virucidal activity of Echinaforce®, an Echinacea purpurea preparation, against coronaviruses, including common cold coronavirus 229E and SARS-CoV-2. *Virology* 2020 Sep 9;17(1):136.
2. Kolev et al. Echinacea purpurea for the Long-term Prevention of Viral Respiratory Tract Infections during COVID-19 Pandemic: A Randomized, Open, Controlled, Exploratory Clinical Study. *medRxiv* 2021.12.10.21267582; doi: <https://doi.org/10.1101/2021.12.10.21267582>
3. Nicolussi S, Gancitano G, Klein P, Stange R, Ogal M. Echinacea as a Potential Weapon against Coronavirus Infections: A Mini-Review of Randomized Controlled Trials. GA conference (Poster), 2021, Bonn, Germany.
4. Vimalanathan S, et al. Broad antiviral effects of Echinacea purpurea against SARS-CoV-2 variants of concern and potential mechanism of action. *bioRxiv* 2021.12.12.472255; doi: <https://doi.org/10.1101/2021.12.12.472255>

Conclusion

Echinaforce® extract shows significant antiviral activity and reduces the risk of viral respiratory infections, including SARS-CoV-2. By significantly reducing the viral load in infected individuals, it offers a supportive option to existing interventions such as vaccination. The extract could also be a useful option for controlling existing and future mutations of the SARS-CoV-2 virus, whereas further studies are certainly warranted.

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