

Cone Purple Flower (*Echinacea purpurea.*) Effect on Respiratory Viral Infections (Brief Review Study): Could it be a Possible Solution to SARS-COV-2 and Other Viral Infection Pandemic Lockdown?

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Abstract

Respiratory tract infections are the most frequently encountered illnesses in the world. It costs billion of US dollars every year to human kind. This costs include the medical ambulatorial care, medicines, costs of hospital stay for severe infections and the loss of work and school days. Estimated costs in the United States for the common cold are \$40 billion per year and over \$87 billion per year for influenza. Some viruses such as influenza A (H3N2 and H1N1) and influenza B can be avoided by mass immunization, however some common cold virus and coronavirus do not have an available vaccine yet, for this reason is important to find another ways of preventing this diseases or alleviate the course of malady in case of acute infection. The objective of this article is to investigate the potential of EP on acute viral respiratory disease treatment including the possibility of use against sars-cov-2 disease. Twelve different papers concerning this theme were found and selected in mesh database. This studies revealed that EP has an antiviral and immunomodulatory activity against membrane containing virus, for this reason it is a potential weapon in fight against SARS-COV-2, but some specific studies must be conducted to evaluate and prove this hypothesis.

Keywords: *Echinacea purpurea*; COVID19; Acute Respiratory Distress; SARS-COV-2

Introduction

Respiratory tract infections are the most frequently encountered illnesses in the world. These infections encompass common cold and influenza, both of which may be manifested by a variety of symptoms from slight nasal stuffiness and an itching throat, to headaches, chesty cough and fever [1].

Cold and flu are caused by a wide variety of viruses such as the rhinovirus, coronavirus, respiratory syncytial virus (RSV), metapneumovirus, Bocca virus and finally, the parainfluenza and Influenza viruses [2].

Acute respiratory infections costs billion of US dollars every year to human kind. This costs include the medical ambulatorial care, medicines, costs of hospital stay for severe infections and the loss of work and school days [3]. Estimated costs in the United States for the common cold are \$40 billion per year and over \$87 billion per year for influenza [4].

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Furthermore, viruses including emerging virus epidemics, such as the 2002 - 2003 severe acute respiratory syndrome coronavirus (SARS-COV) and the recently emerged SARS-COV-2 occurs during the winter months, indicating that the winter environment promotes the spread of a variety of respiratory virus infections [4].

Some viruses such as influenza A (H3N2 and H1N1) and influenza B can be avoided by mass immunization prior to winter months, however some common cold virus and coronavirus do not have an available vaccine yet, for this reason is important to find another ways of preventing this diseases or alleviate the course of malady in case of acute infection [5].

Some natural medications are described as having beneficial effects against the acute viral respiratory infections. The most famous medicines of these groups are the extracts of *Echinacea purpurea* (EP) plant parts (aerial and roots parts), the most popular medication is called Echinaforce® [6].

These natural medications can be a potential weapon to be used in prevention and treatment of respiratory acute viral maladies.

Objective of the Study

The objective of this article is to investigate the potential of EP on acute viral respiratory disease treatment including the possibility of use against sars-cov-2 disease.

Methods

The investigators used the pubmed mesh database tool and performed a search using the terms: *Echinacea purpurea* “and” acute respiratory viral infection treatment.

The articles of last three decades were chosen, selected, accessed, evaluated and summarized to obtain information concerning the results of EP use on acute respiratory viral conditions.

Results

Twelve different papers concerning this theme were found and selected in mesh database. The investigators found one review paper that explain the effects of EP in respiratory infectious diseases treatment. Another five experimental articles exploring the effects in animal models and cell cultures. One article describes a cohort study of use EP preparations in athletes to prevent common cold. The investigators have found three randomized controlled trials, two of these are placebo controlled to investigate the use of EP on treatment and prevention of colds and one paper compare the effects of Tamiflu® to the effects of EP preparations on treatment of influenza. Finally, there are two meta-analysis regarding the treatment of common cold with EP.

The review paper [6] describes the EP extract called Echinaforce® and its capacity of resolve some respiratory viral diseases. According to this study, the medication mentioned previously has *in vitro* anti-viral action against the influenza viruses (H3N2, H1N1, H5N1, H7N7 and S-OIV), coronaviruses and parainfluenza viruses. This antiviral property is due to the capacity of the extract to modify the virus membrane’s surfaces creating a difficulty to enter the cell and to the interference promoted by the extract at the earlier virus replication step (cellular infection). The EP extract did not affect the capability of viral intracellular replication. The continuous passaging of influenza viruses in extract solution did not generated viral resistance as it happens with Tamiflu® [6].

The Cohort study [7] was performed with 80 patients with ages varying from 18 to 75 years old (mean: 40.5 years, n = 41 women, n = 39 men). All of the participants were athletes that practice an amount of 4.3 periods/week of minimum time of 30 minutes of intense physical activity. The excess of hard physical activity promotes immune deficiency that favors the athletes become common cold sick,

specially during winter months. The participants were supplemented with 2 tablets of 750 mg EP extract daily for at least 8 weeks. At the end of study 71% of participants were free of cold, only 3% of them had 1 cold episode and 26% had 2 cold episodes. Adverse drug effect characterized by cutaneous rash and gastrointestinal complaint was documented in only one patient at day 51 of treatment. According to the authors the results were positive for cold protection proofing the efficiency of EP for prevention purposes [7].

The animal model and cell culture studies give us detailed information regarding the mechanisms of EP extract mechanisms of action. The first study₉ evaluated the effect of EP extract in different kinds of cell cultures infected with different kinds of respiratory viruses. The *Echinacea* extract showed impressive antiviral activity against several membrane containing viruses. Results of a MIC₁₀₀ assay Influenza virus and HSV were very sensitive, giving rise to MIC₁₀₀ < 1.0 µg/mL. Respiratory syncytial virus was also sensitive, but with a significantly higher MIC (2.5 µg/mL), while the non-membrane viruses, rhinovirus types 1A and 14, adenovirus 3 and 11, feline calicivirus, and poliovirus, were resistant to the highest concentration tested (800 µg/mL), although the rhinovirus showed partial inhibition of EP at this concentration. Additional findings suggests that the stimulation of cytokine secretion was evident at all time points, but *Echinacea* showed a complete neutralization of the virus induced levels [8].

The second study in animal model [9] compared the effects of EP extracts in influenza (H1N1) infected mice to the control group of infected mice that did not received it. The investigators realized that the untreated mice had more weight loss than the mice that received EP (weight loss of 0.57 g/day [95%CI: 0.50, 0.63] versus 0.27 g/day [95%CI: 0.20, 0.33]). Mice treated with EP did not show differences in lung viral titers between the two groups although EP treated mice had shown lower blood levels of cytokines KC, IFN γ and IL-10 [9]. This fact could explain the immunomodulatory effect of the plant extract.

The third animal model experiment [10] was performed using different groups of mice. The intervention groups received different doses of EP extract daily in dietary for seven days, the control group received dietary without EP extract. The mice were immunized with sheep red blood cell antigen (SBRC). The mice were sacrificed and their spleens were evaluated. The mice treated with EP produced higher levels of anti-SBRC antibodies compared to control group and had a higher mitogen induced proliferation of their splenic lymphocytes that was proportional to the EP doses ($p < 0.0001$) [10].

The fourth animal experiment [11] consist on a study that investigate the behavior of mice macrophages cell cultures to HSV viral infection in presence of EP extract and in absence of it. The cells that was treated with the extract prior to infection do not show increase in TNF α and TNF β levels compared with the control group. An additional effect was the increase of nitric oxide synthase protein in treated cell after viral infection. This suggests that the immunomodulation promoted by EP is related to the nitric oxide tissue production [11].

The last animal experiment [12] is the evaluation of bronchial epithelial cell cultures response to exposure of EP extract and the pathogens: influenza H3N2 virus, *Staphylococcus aureus* and *Haemophilus influenzae* simulating a lung superinfection caused by viral and bacterial agents. The authors compared the group of EP treated cell and the control group. They realized that the influenza viral infection enhance the adhesion between bronchial epithelial cells and the bacteria by the expression of intracellular adhesion molecules I (ICAM-1), fibronectin and platelet activating factor receptor (PAFr). The treated cells expressed a reduction of these molecules blocking the bacterial adhesion to each cells and promoting a protective effect against secondary bacterial infection [12].

Investigators have found three different randomized controlled trials. The first one [13] is a double blind randomized placebo controlled trial that considered the beneficial effect of EP to prevent common cold. This study had 673 participants randomized in two groups, the intervention and the control. There was no statistical difference between the incidence of colds among the two arms. The conclusion was that EP do not have positive effects regarding prevention of colds [13].

Another randomized controlled trial investigate the hole of EP preparation on treatment of common cold [14]. This study was performed with 713 participants with common cold symptoms divided in groups that received EP tablets, blinded EP tablets, blinded placebo

tablets and no pill. The primary outcomes evaluated were the severity of symptoms and duration of pathological process. There were a tendency to less severe symptoms and shorter disease in the two EP groups, but there was no statistical significance. The secondary outcomes were the count of neutrophil and IL-8 in nasal wash material. There was a tendency of increased values of this two substances in EP groups but with no statistical significance [14].

The last randomized controlled trial [15] compare the effects of EP to the effects of Tamiflu® on patients with confirmed influenza viral infection. The study enrolled 237 participants divided in two arms. One arm received EP and another arm received oseltamivir as placebo pills. The recovery of symptoms was observed in two groups at 1,5% versus 4.1% after 1 day, 50.2% versus 48.8% after 5 days and 90.1% versus 84.4% after 10 days of treatment of EP and Tamiflu® respectively. The incidence of complications was lower in EP group (2.46% versus 6.45%; $p = .076$) [15].

Finally, the investigators analyzed two meta-analyses. The first evaluated the effect of EP on prevention and treatment of common cold [16]. An amount of 24 clinical trials (14 prevention, 9 treatment and 1 trial investigate both: prevention and treatment - $N = 2809$ for treatment and $N = 1822$ for prevention) This study shown a weak relation of use EP products and common cold prevention and weak relation between EP use and cold resolution [16].

The last study is a meta-analysis [17] that enrolled 23 trial that evaluated the impact of *Echinacea* products use on incidence and duration of common cold ($n = 1356$ for incidence and $n = 1630$ for duration). The results revealed that the use of EP products reduced the incidence and duration of common cold [17].

Discussion

The EP products have shown anti-viral activity *in vitro* experiments, specially to membrane containing virus such as influenza and coronavirus family [6,8]. Some common cold prevalent virus such as rhinovirus and adenovirus do not have this capacity. For this reason, the randomized trials that evaluated the effects of EP medications in common cold patients do not have significant results.

On the other hand, the same kind of studies that evaluated the extract action against the influenza virus, have shown good results, equivalent to Tamiflu results, with the advantage of less adverse effects and with no virus drug resistance [15].

EP extract has also an immunomodulatory effect that has been well documented in experimental studies [8-11]. In this experiments was proven that respiratory virus such influenza A and B virus induce the infected tissues to produce some cytokines that lead to systemic inflammation and aggravate the lungs aggression. EP seems to has a regulatory activity on this complex mechanism and is a potential drug to use on SARS treatment. Another property of the extract is to minimize the secretion of adhesion proteins at bronchial epithelial surface reducing the capacity of bacterial adhesion leading to a secondary bacterial infection [12].

Nowadays the world is suffering of a pandemic SARS-COV-2 acute respiratory infection. There is no vaccines until this moment and all available treatment do not have high evidence levels of success. For this reason, is important to think of EP extract of a potential weapon that could be used in fight against COVID19. Some specific studies must be done to evaluate and prove this potential.

Conclusion

The EP has antiviral and immunomodulatory effects specially against membrane containing virus. It has a potential to became a weapon in fight against SARS-COV-2, but some specific studies must be conducted to evaluate and prove this hypothesis.

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Disclosure Statement

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Bibliography

1. Rotbart HA and Hayden FG. "Picornavirus infections: a primer for the practitioner". *Archives of Family Medicine* 9.90 (2000): 913-922.
2. Fendrick AM. "Viral respiratory infections due to rhinoviruses: current knowledge, new developments". *American Journal of Therapeutics* 10 (2003): 193-202.
3. Shahan B., *et al.* "Respiratory Conditions: Upper Respiratory Tract Infections". *FP Essentials* 486 (2019): 11-18.
4. Miyu Moriyama., *et al.* "Seasonality of Respiratory Viral Infections". *Annual Review of Virology* 7 (2020): 2.1-2.19.
5. Vinuesa CG., *et al.* "Follicular helper T cells". *Annual Review of Immunology* 34 (2016): 335-368.
6. Andreas Schapowal. "Efficacy and safety of Echinaforce® in respiratory tract infections". *Wiener Medizinische Wochenschrift* 163.3-4 (2013): 102-105.
7. Stephanie Maxine Ross. "A Standardized *Echinacea* Extract Demonstrates Efficacy in the Prevention and Treatment of Colds in Athletes". *Holistic Nursing Practice* 24.2 (2010): 107-109.
8. Manju Sharma., *et al.* "Induction of multiple pro-inflammatory cytokines by respiratory viruses and reversal by standardized *Echinacea*, a potent antiviral herbal extract". *Antiviral Research* 83 (2009): 165-170.
9. Dahlene Fusco., *et al.* "*Echinacea purpurea* aerial extract alters course of influenza infection in mice". *Vaccine* 28.23 (2010): 3956-3962.
10. Bar Bara Joanna Bałan., *et al.* "The modulatory influence of some *Echinacea*-based remedies on antibody production and cellular immunity in mice". *Central European Journal of Immunology* 41.1 (2016): 12-18.
11. David S Senchina., *et al.* "Effects of *Echinacea* Extracts on Macrophage Antiviral Activities". *Phytotherapy Research* 24 (2010): 810-816.
12. Vimalanathan S., *et al.* "Prevention of influenza virus induced bacterial superinfection by standardized *Echinacea purpurea*, via regulation of surface receptor expression in human bronchial epithelial cells". *Virus Research* 233 (2017): 51-59.
13. Ross SM. "*Echinacea purpurea*: A Proprietary Extract of *Echinacea purpurea* Is Shown to be Safe and Effective in the Prevention of the Common Cold". *Holistic Nursing Practice* 30.1 (2016): 54-57.
14. Barrett B., *et al.* "*Echinacea* for treating the common cold: a randomized trial". *Annals of Internal Medicine* 153.12 (2010): 769-777.

15. Ross SM. "Echinacea Formula (Echinaforce® Hotdrink): Effects of a Proprietary *Echinacea* Formula Compared With Oseltamivir in the Early Treatment of Influenza". *Holistic Nursing Practice* 30.2 (2016):122-125.
16. Karsch-Völk M., et al. "Echinacea for preventing and treating the common cold". *The Journal of the American Medical Association* 313.6 (2015): 618-619.
17. Shah SA., et al. "Evaluation of *Echinacea* for the prevention and treatment of the common cold: a meta-analysis". *The Lancet Infectious Diseases* 7.7 (2007): 473-480.

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