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Natural Way Of Boosting Immunity: The Role of Echinacea in Cold Prevention and Treatment - A Literature Review

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Abstract

Echinacea, a widely used herbal remedy derived from the purple coneflower, is renowned for its potential benefits in treating and preventing the common cold. This review examines Echinacea's role in managing cold symptoms, its mechanisms of action, and its efficacy across various species and preparations. Echinacea species, particularly *Echinacea purpurea*, *Echinacea angustifolia*, and *Echinacea pallida*, contain active compounds such as alkamides, caffeic acid derivatives, polysaccharides, and glycoproteins, which contribute to its immunomodulatory, anti-inflammatory, and antiviral properties. Clinical studies demonstrate that Echinacea can modestly reduce the incidence, duration, and severity of colds, though results are variable due to differences in preparation forms (e.g., teas, tinctures, extracts) and study methodologies. Proprietary extracts like Echinaforce® have shown consistent benefits, while other formulations have yielded mixed results. Despite a generally favorable safety profile, including mild gastrointestinal disturbances and rare allergic reactions, the long-term safety, particularly in vulnerable populations, remains under-researched. Future research should focus on standardized formulations, detailed molecular mechanisms, and rigorous clinical trials to better define Echinacea's role in cold management. Overall, while Echinacea offers a promising option for cold prevention and treatment, its use should be informed by evidence-based practices considering formulation, dosage, and individual patient factors.

Introduction

Echinacea, commonly known as the purple coneflower, is a medicinal herb traditionally used to treat respiratory infections such as the common cold, coughs, bronchitis, and certain inflammatory conditions (1). The genus Echinacea comprises several species, including *Echinacea purpurea, Echinacea angustifolia*, and *Echinacea pallida*, which are used in various preparations (2). These preparations are available in multiple forms, such as teas, tinctures, extracts, capsules, and tablets, and are marketed primarily for their potential immune-boosting properties (3). The primary use of Echinacea in modern herbal medicine is for the treatment and prevention of the common cold (4). Echinacea remains widely used in Europe and North America, with annual spending in the United States exceeding \$300 million (2).

The common cold is a viral infection primarily affecting the upper respiratory tract, characterized by symptoms such as a runny nose, cough, and sore throat. Most symptoms resolve within 1 week, but coughs often persist for longer. (5) It is most commonly caused by rhinoviruses, although other viruses like coronaviruses and human metapneumovirus are also significant contributors (6). The common cold is widespread, with adults experiencing 2-4 episodes annually, while children can have twice as many (7). Prevention includes proper hand hygiene and the use of prophylactic measures like probiotics and zinc supplements, which can reduce the frequency and severity of colds (8).

As this review progresses, it will further explore the intricacies of Echinacea in the treatment of the common cold. The exploration of these variables is crucial for understanding Echinacea's role in cold treatment and guiding its evidence-based use in clinical practice. Emerging strategies and research into its broader application could further refine its use in prevention and managing cold symptoms.

Echinacea species and their characteristics

Echinacea comprises several species, each with unique features and characteristics, contributing to its widespread use in herbal medicine, particularly for the prevention and treatment of common colds. The most commonly studied species are *Echinacea purpurea*,

Echinacea angustifolia, and *Echinacea pallida*. *Echinacea purpurea*, a perennial herb, is renowned for its immunostimulatory and anti-inflammatory properties, largely attributed to its active compounds such as alkamides, caffeic acid derivatives, polysaccharides, and glycoproteins (9). These compounds are thought to enhance immune function by modulating cytokine production and improving the activity of natural killer (NK) cells.

In contrast, *Echinacea angustifolia* and *Echinacea pallida* are often used in different forms, such as tinctures and extracts, and they have been traditionally employed for similar purposes, although they may have slightly different phytochemical profiles. For instance, *Echinacea angustifolia* is particularly rich in alkamides and glycoproteins, which are believed to interact with cannabinoid receptors, thus contributing to its immune-modulatory effects (4).

Clinical studies have shown variability in the effectiveness of these species, with some trials suggesting a modest reduction in the incidence and duration of colds, while others show no significant benefit, indicating that the specific preparation and the part of the plant used can significantly influence outcomes (4). Furthermore, *Echinacea purpurea* is often preferred due to its well-documented pharmacological activities, although the efficacy of each species may vary depending on the extraction method and the specific conditions being treated (10).

Despite these differences, all three species share common characteristics such as their ability to act as immune boosters and their general safety profile. However, some studies have reported adverse effects, particularly with *Echinacea purpurea*, including gastrointestinal disturbances and allergic reactions, which suggests that more research is needed to fully understand the safety and efficacy of these species in diverse populations (11).

Mechanism of action

Echinacea, particularly *Echinacea purpurea*, is well-recognized for its immunomodulatory, anti-inflammatory, and antiviral properties, which are particularly beneficial in the treatment and prevention of cold-related symptoms and respiratory infections. The key active ingredients in Echinacea include various secondary metabolites such as alkamides, caffeic acid derivatives (e.g., cichoric acid), polysaccharides, and glycoproteins (9). Alkamides are known to interact with cannabinoid receptors, particularly CB2 receptors, which modulate immune responses by influencing cytokine release and enhancing the activity of natural killer (NK) cells and macrophages. These immune cells are crucial in the body's defense against viral pathogens, making Echinacea a valuable adjunct in managing cold symptoms (12).

Caffeic acid derivatives, such as cichoric acid, contribute to Echinacea's antioxidant properties and play a role in the inhibition of hyaluronidase, an enzyme that degrades hyaluronic acid in the extracellular matrix, potentially limiting the spread of infections (9). Polysaccharides in Echinacea also enhance the immune response by increasing the production of cytokines like tumor necrosis factor-alpha (TNF- α) and interleukins, which are vital for initiating and regulating immune responses (12).

Echinacea's role in reducing the incidence and severity of respiratory infections has been supported by clinical studies that show its efficacy in decreasing the recurrence of these infections, particularly in individuals with compromised immune systems or under high stress (12). Furthermore, Echinacea exhibits direct antiviral activity, which may further reduce the risk of recurrent infections and complications such as pneumonia and otitis media (13).

Despite the extensive research on Echinacea, there are still gaps in our understanding of its full mechanism of action. Future studies should focus on the detailed molecular interactions of Echinacea's active compounds with specific immune receptors and pathways, as well as the long-term effects of Echinacea supplementation on immune health (14).

Echinacea in the prevention of the common cold

Echinacea has been scrutinized in various scientific studies for its role in the prevention of the common cold. Karsch-Völk et al. (2014) conducted a comprehensive review of 24 doubleblind trials involving 4,631 participants to assess the efficacy and safety of Echinacea compared to placebo. This study highlighted the variability in outcomes based on different Echinacea preparations, yet provided evidence for some beneficial effects (4). Similarly, a large clinical trial by Ross (2016) demonstrated that a proprietary Echinacea purpurea extract (Echinaforce) could reduce the total number of cold episodes, duration of colds, and cold episodes requiring additional medication over a 4-month period, suggesting a positive risk-to-benefit ratio when used for the prevention of the common cold. This study found that long-term use of Echinacea was associated with a reduction in the total number of cold episodes, a decrease in the number of days with colds, and fewer cold episodes requiring additional medication. Notably, Echinacea was particularly effective in preventing virally confirmed colds and recurrent infections, with its efficacy increasing in relation to adherence to the prescribed regimen (15). Echinacea's historical context is also noteworthy, with its popularity in Europe and the United States as a common herbal remedy, despite controversies regarding its effectiveness in cold and flu treatment highlighted by Tierra (2008) (16).

Furthermore, Shah et al. (2007) provided a meta-analysis evaluating the impact of Echinacea on the incidence and duration of the common cold, concluding that Echinacea significantly decreased the odds of developing the common cold by 58% and reduced the duration of a cold by 1.4 days (17). Another meta-analysis focused on experimental rhinovirus infections by Schoop et al. (2006) supported the potential benefits of Echinacea extracts in preventing symptomatic development of an experimentally induced cold (18).

Additionally, The study conducted by Ogal et al. (2021) explored the effectiveness of Echinacea in preventing viral respiratory tract infections (RTIs), their secondary bacterial complications, and in reducing the necessity for antibiotic prescriptions among children. The randomized, blinded, controlled trial administered 400 mg of freshly harvested Echinacea purpurea extract (Echinaforce® Junior tablets) or 50 mg of vitamin C as a control, three times daily to children aged between 4 and 12 years. The intervention notably resulted in a significant reduction in RTI episodes; children treated with Echinacea experienced 429 days of cold symptoms compared to 602 days in children given vitamin C, marking a 32.5% decrease in the occurrence of RTIs in the Echinacea group. Moreover, the study reported a substantial reduction in antibiotic prescriptions, with Echinacea users requiring 76.3% fewer antibiotic courses than the control group. In line with these findings, the rate of RTI-related complications like otitis media, sinusitis, or pneumonia was significantly lower among those who received Echinacea. Notably, Echinacea substantially reduced the incidence of influenza and enveloped virus infections, further underscoring its preventative efficacy against viral infections. Despite this, adverse events were infrequent, with only three incidents potentially related to Echinacea use, suggesting a favorable safety profile for its use in pediatric populations for RTI prevention. (19)

Echinacea in the treatment of the common cold

The effectiveness of Echinacea in relieving symptoms and treating the common cold has been a subject of research across various studies, yielding mixed results. Fashner et al. (2012) found that in children, Echinacea, along with other treatments such as inhaled corticosteroids and oral prednisolone, are ineffective. In adults, however, some herbal preparations, including Echinacea purpurea, have been observed to improve symptoms (7). Mousa (2017) suggests that while traditional and alternative therapies such as Echinacea have been used for viral respiratory illnesses, including the common cold, scientific evidence supporting their effectiveness varies, with some natural therapies like oral zinc showing more consistent benefits in terms of reduction in the length and severity of cold symptoms (8).

Giles et al. (2000) provided a critical evaluation of Echinacea's purported efficacy for treating or preventing upper respiratory tract infections. They acknowledged the herb's widespread use and considered it to have immunostimulating activity, but also highlighted the unclear results due to methodological flaws in existing studies (20). Caruso and Gwaltney's (2005) structured review of clinical trials examining Echinacea for the common cold indicated that its therapeutic effectiveness has not been conclusively established, with the most common criterion not met being the proof of blinding in studies (2). Knight (2005), reflecting on the economics and utility of Echinacea in cold treatment, further emphasized the challenges in justifying Echinacea's use given the mild and self-limiting nature of the common cold and the limited evidence supporting its effectiveness across the spectrum of cold viruses (21).

Effectiveness of the various forms of Echinacea preparations

The scientific research exploring the effectiveness of different forms of Echinacea preparations in treating common cold symptoms presents a varied landscape of medicinal utility and efficacy. Percival (2000) elucidates the traditional use of Echinacea in treating respiratory and some inflammatory conditions, pointing towards a necessity for future research to decipher the species and plant parts (roots versus upper parts) for optimal efficacy. The study suggests that certain preparations of Echinacea are indeed effective in reducing the duration and severity of symptoms, hinting at a variety-dependent effect on the immune system (1).

Further exploring the effectiveness of Echinacea purpurea, Signer et al. (2020) delve into its antiviral potential against human coronaviruses, including SARS-CoV-2, demonstrating its virucidal activity. While this study primarily focuses on the in vitro virucidal properties of Echinacea purpurea (Echinaforce®) against coronaviruses, it adds a layer to the narrative of Echinacea's antiviral capabilities (22). The research by Jawad et al. (2012) supports the usage of Echinacea purpurea extract in common cold prevention, demonstrating a reduction in cold episodes and an enhanced preventive effect on recurrent infections, particularly for enveloped viruses (23).

Brinkeborn et al. (1999) provide insights into a comparative analysis of different Echinacea purpurea preparations, indicating that specific concentrations and mixtures (notably, Echinaforce® and its higher concentration preparations) show significant effectiveness over other Echinacea extracts or placebo in the acute treatment of common cold (24). Similarly, Goel et al. (2005) report on Echinilin[™], a standardized Echinacea purpurea preparation, highlighting its systemic immune response enhancement during a common cold and suggesting mechanisms through sustained increases in white blood cells and neutrophil activity (25).

Side effects of Echinacea

The evaluation of Echinacea use and its side effects, as presented in various clinical trials, illustrates a nuanced safety profile for this popular herbal remedy commonly used for the treatment of the common cold. Yale and Liu's (2004) investigation into Echinacea purpurea for cold treatment did not specifically discuss adverse effects within its abstract, focusing instead on efficacy outcomes (26). Similarly, Grimm and Müller's (1999) randomized trial comparing the effects of the Echinacea purpurea fluid extract on the incidence and severity of colds did not find significant differences between treatment and placebo groups in terms of side effects, observed in 20% of the Echinacea group and 13% of the placebo group (27). Barrett et al. (2002) evaluated an unrefined combination of Echinacea purpurea herb and root and reported no significant adverse effects, emphasizing the investigation into efficacy rather than safety profile (28). Another study by Naser et al. (2005), which involved a mixture containing Echinacea, reported no adverse events across the trial, thereby reinforcing the assumed safety of Echinacea in treating upper respiratory tract infections (29). Lastly, Barrett et al. (2010) in a comprehensive trial on Echinacea's benefits for the common cold, did mention the monitoring of side effects but did not detail specific adverse effects, focusing instead on the primary outcomes related to the efficacy of Echinacea in treating the common cold (30).

Conclusion

The review of Echinacea's role in the prevention and treatment of the common cold provides a comprehensive understanding of its potential benefits, mechanisms of action, varying efficacies among different species and preparations, and overall safety profile. The evidence

suggests that Echinacea, particularly *Echinacea purpurea*, has a modest yet clinically relevant effect in reducing the incidence, duration, and severity of cold symptoms when used consistently and as per standardized dosing regimens. This effect is primarily attributed to its immunomodulatory, anti-inflammatory, and antiviral properties, driven by its active compounds, such as alkamides, caffeic acid derivatives, polysaccharides, and glycoproteins. These compounds interact with immune pathways, enhancing the activity of natural killer cells, cytokine production, and inhibition of viral spread, which collectively contribute to its therapeutic effects against respiratory infections.

However, the review also highlights the variability in outcomes observed across clinical studies, which can be attributed to differences in the species used (e.g., *Echinacea purpurea, Echinacea angustifolia*, and *Echinacea pallida*), parts of the plant utilized, preparation forms (e.g., teas, tinctures, extracts, capsules, and tablets), and study designs. The variability in the effectiveness of Echinacea in treating the common cold suggests that the specific formulation, extraction method, and dosage play crucial roles in its efficacy. For instance, studies focusing on proprietary extracts like Echinaforce® have demonstrated consistent benefits in reducing cold episodes and preventing recurrent infections, while other formulations show more inconsistent results. This underscores the need for standardization in Echinacea preparations and further research to determine optimal dosing and formulations for different populations.

Despite the promising findings, the current body of research still has limitations. Some studies exhibit methodological flaws, such as small sample sizes, lack of proper blinding, and heterogeneous study designs, which can lead to conflicting results. Furthermore, the long-term safety profile of Echinacea, particularly in vulnerable populations such as children, pregnant women, and individuals with chronic illnesses, remains underexplored. Although Echinacea is generally considered safe with a low incidence of adverse effects, such as mild gastrointestinal disturbances and allergic reactions, these findings are not universally observed across all studies. Therefore, caution is advised when recommending Echinacea for routine use, especially in populations with known allergies or autoimmune disorders.

The review of Echinacea's effectiveness in treating the common cold also reveals gaps in our understanding of its mechanism of action. While the immunostimulatory and antiviral properties of Echinacea are well-documented, the precise molecular interactions and pathways involved require further elucidation. Future studies should focus on detailed molecular-level investigations to better understand how Echinacea's active compounds modulate immune function and influence viral replication and spread. Moreover, well-designed randomized controlled trials with standardized preparations and well-defined outcome measures are essential to solidify the evidence base for Echinacea's use in clinical practice.

In conclusion, while Echinacea presents a promising herbal option for the prevention and management of the common cold, its use should be guided by evidence-based practice, considering the preparation type, dosage, patient-specific factors, and existing comorbidities. Healthcare providers should be informed about the variability in efficacy and potential adverse effects to provide balanced recommendations to patients. Continued research, especially high-quality clinical trials and mechanistic studies, is crucial to fully realize Echinacea's therapeutic potential and integrate it into mainstream cold prevention and treatment strategies.

Disclosure

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Bibliography:

- Percival, S. S. (2000). Use of echinacea in medicine. *Biochemical Pharmacology*, 60(2), 155–158. <u>https://doi.org/10.1016/s0006-2952(99)00413-x</u>
- Caruso, T. J., & Gwaltney, J. M. (2005). Treatment of the Common Cold with Echinacea: A Structured Review. *Clinical Infectious Diseases*, 40(6), 807–810. <u>https://doi.org/10.1086/428061</u>
- Dobrange, E., Peshev, D., Loedolff, B., & Van Den Ende, W. (2019b). Fructans as immunomodulatory and antiviral agents: the case of echinacea. *Biomolecules*, 9(10), 615. <u>https://doi.org/10.3390/biom9100615</u>
- Karsch-Völk, M., Barrett, B., Kiefer, D., Bauer, R., Ardjomand-Woelkart, K., & Linde, K. (2014). Echinacea for preventing and treating the common cold. *Cochrane Library*, 2014(7). <u>https://doi.org/10.1002/14651858.cd000530.pub3</u>
- 5. Common cold. (2011, March 16). PubMed. https://pubmed.ncbi.nlm.nih.gov/21406124/
- Heikkinen, T., & Järvinen, A. (2003). The common cold. *The Lancet*, 361(9351), 51– 59. <u>https://doi.org/10.1016/s0140-6736(03)12162-9</u>
- Treatment of the common cold in children and adults. (2012, July 15). PubMed. https://pubmed.ncbi.nlm.nih.gov/22962927/
- Mousa, H. A. (2016). Prevention and treatment of Influenza, Influenza-Like Illness, and Common Cold by herbal, complementary, and natural therapies. *Journal of Evidence-Based Complementary & Alternative Medicine*, 22(1), 166–174. <u>https://doi.org/10.1177/2156587216641831</u>
- Saeidnia, S., Manayi, A., & Vazirian, M. (2015b). Echinacea purpurea: Pharmacology, phytochemistry and analysis methods. *Pharmacognosy Reviews/Bioinformatics Trends/Pharmacognosy Review*, 9(17), 63. <u>https://doi.org/10.4103/0973-7847.156353</u>
- Wagner, L., Cramer, H., Klose, P., Lauche, R., Gass, F., Dobos, G., & Langhorst, J. (2015). Herbal Medicine for Cough: a Systematic Review and Meta-Analysis. *Complementary Medicine Research*, 22(6), 359–368. <u>https://doi.org/10.1159/000442111</u>

- Barrett, B., Rakel, D., Chewning, B., Marchand, L., Rabago, D., Brown, R., Scheder, J., Schmidt, R., Gern, J. E., Bone, K., Thomas, G., Barlow, S., & Bobula, J. (2007). Rationale and methods for a trial assessing placebo, echinacea, and Doctor-Patient interaction in the Common Cold. *EXPLORE*, *3*(6), 561–572. https://doi.org/10.1016/j.explore.2007.08.001
- Schapowal, A., Klein, P., & Johnston, S. L. (2015). Echinacea reduces the risk of recurrent respiratory tract infections and complications: A Meta-Analysis of Randomized Controlled trials. *Advances in Therapy*, 32(3), 187–200. <u>https://doi.org/10.1007/s12325-015-0194-4</u>
- 13. Rondanelli, M., Miccono, A., Lamburghini, S., Avanzato, I., Riva, A., Allegrini, P., Faliva, M. A., Peroni, G., Nichetti, M., & Perna, S. (2018). Self-Care for Common Colds: The Pivotal Role of Vitamin D, Vitamin C, Zinc, and Echinacea in Three Main Immune Interactive Clusters (Physical Barriers, Innate and Adaptive Immunity) Involved during an Episode of Common Colds—Practical Advice on Dosages and on the Time to Take These Nutrients/Botanicals in order to Prevent or Treat Common Colds. *Evidence-based Complementary and Alternative Medicine*, 2018, 1–36. https://doi.org/10.1155/2018/5813095
- 14. Nahas, R., & Balla, A. (2011, January 1). Complementary and alternative medicine for prevention and treatment of the common cold. PubMed Central (PMC). <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3024156/</u>
- Ross, S. M. (2016). Echinacea purpurea. *Holistic Nursing Practice*, 30(1), 54–57. https://doi.org/10.1097/hnp.00000000000130
- 16. Tierra, M. (2008). Echinacea. *Journal of Herbal Pharmacotherapy*, 7(2), 79–89. https://doi.org/10.1080/j157v07n02_06
- Shah, S. A., Sander, S., White, C. M., Rinaldi, M., & Coleman, C. I. (2007). Evaluation of echinacea for the prevention and treatment of the common cold: a metaanalysis. *The Lancet Infectious Diseases*, 7(7), 473–480. <u>https://doi.org/10.1016/s1473-3099(07)70160-3</u>
- Schoop, R., Klein, P., Suter, A., & Johnston, S. L. (2006). Echinacea in the prevention of induced rhinovirus colds: A meta-analysis. *Clinical Therapeutics*, 28(2), 174–183. <u>https://doi.org/10.1016/j.clinthera.2006.02.001</u>
- 19. Ogal, M., Johnston, S. L., Klein, P., & Schoop, R. (2021). Echinacea reduces antibiotic usage in children through respiratory tract infection prevention: a

randomized, blinded, controlled clinical trial. *European Journal of Medical Research*, 26(1). <u>https://doi.org/10.1186/s40001-021-00499-6</u>

- 20. Giles, J. T., Palat, C. T., Chien, S. H., Chang, Z. G., & Kennedy, D. T. (2000). Evaluation of echinacea for treatment of the common cold. *Pharmacotherapy the Journal of Human Pharmacology and Drug Therapy*, 20(6), 690–697. <u>https://doi.org/10.1592/phco.20.7.690.35173</u>
- Knight, V. (2005). Echinacea treatment for the common cold. *Clinical Infectious Diseases*, 40(6), 811–812. <u>https://doi.org/10.1086/428063</u>
- Signer, J., Jonsdottir, H. R., Albrich, W. C., Strasser, M., Züst, R., Ryter, S., Ackermann-Gäumann, R., Lenz, N., Siegrist, D., Suter, A., Schoop, R., & Engler, O. B. (2020). In vitro virucidal activity of Echinaforce®, an Echinacea purpurea preparation, against coronaviruses, including common cold coronavirus 229E and SARS-CoV-2. *Virology Journal*, 17(1). <u>https://doi.org/10.1186/s12985-020-01401-2</u>
- 23. Jawad, M., Schoop, R., Suter, A., Klein, P., & Eccles, R. (2012). Safety and Efficacy Profile ofEchinacea purpureato Prevent Common Cold Episodes: A Randomized, Double-Blind, Placebo-Controlled Trial. *Evidence-based Complementary and Alternative Medicine*, 2012, 1–7. <u>https://doi.org/10.1155/2012/841315</u>
- 24. Brinkeborn, R., Shah, D., & Degenring, F. (1999). Echinaforce® and other Echinacea fresh plant preparations in the treatment of the common cold. *Phytomedicine*, 6(1), 1–6. <u>https://doi.org/10.1016/s0944-7113(99)80027-0</u>
- 25. Goel, V., Lovlin, R., Chang, C., Slama, J. V., Barton, R., Gahler, R., Bauer, R., Goonewardene, L., & Basu, T. K. (2005). A proprietary extract from the echinacea plant (Echinacea purpurea) enhances systemic immune response during a common cold. *Phytotherapy Research*, 19(8), 689–694. <u>https://doi.org/10.1002/ptr.1733</u>
- 26. Yale, S. H., & Liu, K. (2004). Echinacea purpurea Therapy for the Treatment of the Common Cold. Archives of Internal Medicine, 164(11), 1237. <u>https://doi.org/10.1001/archinte.164.11.1237</u>
- 27. Grimm, W., & Müller, H. H. (1999). A randomized controlled trial of the effect of fluid extract of Echinacea purpurea on the incidence and severity of colds and respiratory infections * * Access the "Journal Club" discussion of this paper at

http://www.elsevier.com/locate/ajmselect/. *The American Journal of Medicine*, *106*(2), 138–143. https://doi.org/10.1016/s0002-9343(98)00406-9

- Barrett, B. P., Brown, R. L., Locken, K., Maberry, R., Bobula, J. A., & D'Alessio, D. (2002). Treatment of the Common Cold with Unrefined Echinacea. *Annals of Internal Medicine*, 137(12), 939. <u>https://doi.org/10.7326/0003-4819-137-12-200212170-00006</u>
- Naser, B., Lund, B., Zepelin, H. H. H., Köhler, G., Lehmacher, W., & Scaglione, F. (2005). A randomized, double-blind, placebo-controlled, clinical dose-response trial of an extract of Baptisia, Echinacea and Thuja for the treatment of patients with common cold. *Phytomedicine*, *12*(10), 715–722. https://doi.org/10.1016/j.phymed.2005.03.002
- Barrett, B., Brown, R., Rakel, D., Mundt, M., Bone, K., Barlow, S., & Ewers, T. (2010). Echinacea for treating the common cold. *Annals of Internal Medicine*, *153*(12), 769. https://doi.org/10.7326/0003-4819-153-12-201012210-00003