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Recent Advances and Future Directions in Echinacea purpurea Research: A Comprehensive Review

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Abstract: *Echinacea purpurea* (L.) Moench is a well-known medicinal plant widely used in traditional medicine due to its immunomodulatory potential. This review provides an integrated and updated assessment of its phytochemical composition and pharmacological activities, with a particular focus on its application in modern medicine. Bioactive constituents such as polysaccharides, alkamides, flavonoids, and phenolic acid derivatives have been shown to enhance immune function and exhibit anti-inflammatory, antioxidant, antiviral, and antibacterial properties. Notably, this paper discusses the underlying mechanisms of action—including immune cell activation, modulation of inflammatory pathways, and reduction of oxidative stress—by incorporating recent clinical data not fully addressed in earlier reviews. Although *E. purpurea* is supported by scientific evidence as a natural immune enhancer, long-term use and high doses may cause overstimulation, allergic reactions, or drug interactions. Therefore, further clinical studies are essential to fully explore its therapeutic potential and safety profile.

Keywords: *Echinacea purpurea*, Echinacea, biological activity, immune system health

INTRODUCTION

Traditional medical practices have aimed to treat health problems by using plants for thousands of years. Many cultures around the world have treated diseases using medicinal plants, and these practices have contributed to the foundations of modern medicine over time. One of the most important aspects of traditional medicine is that it supports the body's healing processes by utilizing the natural properties of plants (1-3).

Herbal treatments are widely used, especially in traditional medical systems of Asian, African and American origin. Herbal treatments generally aim to prevent, cure and relieve symptoms of diseases. For instance, plants such as *Echinacea* are used to strengthen the immune system, while ginger and mint are known to alleviate digestive problems. In addition to plants in traditional medicine, herbal extracts are consumed in the form of teas, tinctures, and oils. Moreover, medicinal plants not only treat physical diseases, but are also used to support mental and emotional health. The use of plants is often based on providing balance; for example, plants such as lavender oil, which reduces stress, and sage, which has a calming effect, help to improve emotional balance. These traditional approaches are widely used as complementary treatments alongside modern pharmaceutical drugs(4-6). However, although traditional herbal treatments are widely used among the public, scientific research and clinical trials are of great importance regarding the effectiveness and safety of these treatments. Scientific studies have revealed that the chemical components contained in plants may have anti-inflammatory and antibacterial properties that may have an effect on the immune system. Therefore, traditional herbal treatment methods can become an important health tool when supported by scientific findings (7-14).

Echinacea is a plant genus belonging to the Asteraceae family and native to North America. These plants are especially known for their potential to strengthen the immune system and are widely used among natural remedies among the public. *Echinacea* species have been used in traditional medicine to treat infections, relieve colds and increase immune function. *Echinacea* is usually consumed with its roots, flowers and leaves, and these parts are transformed into pharmaceutical products to provide various therapeutic properties. Traditionally, *E. purpurea* has been used by Native American tribes such as the Sioux and Cheyenne for a variety of ailments. These include treating respiratory tract infections, coughs, sore throats, toothaches, and snake bites. Root poultices were commonly applied to wounds, burns, and insect stings, while teas made from aerial parts were consumed to reduce fever and support general health. In European herbal medicine, *E. purpurea* preparations were used as general tonics and anti-infective remedies. Its use expanded during the 19th and 20th centuries as a natural alternative to antibiotics before the advent of modern pharmaceuticals. These widespread applications reflect the plant's historical importance in ethnobotany and support ongoing pharmacological investigations into its therapeutic Potential (9, 15-17).

The *Echinacea* genus generally consists of four main species as known especially medicinal herbs: *E. purpurea*, *E. angustifolia, E. pallida*, and *E. tennesseensis*. Each species has

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different botanical characteristics, environmental requirements, and medicinal uses. *Echinacea* plants attract attention with their large and showy purple, pink, or white flowers, and also have strong antioxidant and anti-inflammatory effects. In addition, the roots of echinacea plants are rich in sugars, alcohol acids, polysaccharides, flavonoids, and alkaloids, which strengthen the immune system and increase the body's resistance to diseases. This article will focus on the botanical characteristics, ecological requirements, and especially medicinal benefits of echinacea species, and will also discuss in detail the areas of use of these plants in modern medicine (16, 18-20).

This review provides an updated and integrative analysis of *Echinacea purpurea* (L.) Moench, focusing on its chemical constituents, pharmacological activities, and mechanisms of action. While a recent review by Burlou-Nagy et al. (21) offers a broad summary of phytochemistry and bioactivity in E. purpurea, our work goes further by incorporating in-depth discussions of immunomodulatory signaling pathways, newly published clinical evidence, and a critical evaluation of safety and usage limitations within modern therapeutic contexts.

METHODOLOGY

A comprehensive literature review was carried out using major databases including PubMed, Scopus, Web of Science, and Google Scholar. The search focused on studies published between January 2000 and March 2025. Keywords such as “Echinacea purpurea,” “phytochemistry,” “pharmacological activity,” “immune modulation,” “clinical trials,” and related terms were used to identify relevant literature.

Studies were selected based on the following inclusion criteria: peer-reviewed original articles, systematic reviews, and clinical trials written in English and directly related to the chemical composition, pharmacological effects, or clinical applications of Echinacea purpurea. Non-peer-reviewed materials, unrelated studies, and duplicates were excluded.

After the removal of duplicates, titles and abstracts were screened, followed by full-text evaluation for relevance. Extracted data were organized based on chemical categories, pharmacological mechanisms, and therapeutic significance. This systematic approach ensured that the review reflects up-to-date and scientifically sound findings.

This methodological framework ensured that the content of this review is based on credible and recent scientific findings, allowing for a balanced and evidence-based synthesis of current knowledge on *E. purpurea*.

Phytochemistry of *Echinacea purpurea*

The effects of *E. purpurea* on the immune system are due to the various bioactive components it contains. The main chemical components of *E. purpurea* and the effects of these components on the immune system are shown in Table 1.

Table (1): Chemical components of *Echinacea purpurea*

Components	Chemical Types	Effect on Immunity
Polysaccharides	Complex carbohydrates	Macrophage activation increases proinflammatory cytokine release.
Alkamides	Lipophilic compound	Increases natural killer (NK) cell activity, anti-inflammatory.
Caffeic acid derivatives	Phenolic compound	Provides antioxidant effects, neutralizes free radicals.
Chicoric acid	Phenolic acid	It reduces cellular oxidative stress.
Flavonoids	Polyphenol	It has antiviral and antimicrobial properties.
Essential oils	Terpenoid compounds	It has antiseptic and immune-supporting effects.
Component	Chemical Type	Effect on Immunity

* Note: Detailed scientific references corresponding to each compound listed in Table 1 are provided at the end of their respective explanatory paragraphs in the main text (Chemical Components section).

E. purpurea, a plant renowned for its medicinal properties, contains a variety of bioactive compounds that contribute to its therapeutic effects. Detailed chemical analyses of this plant have identified numerous classes of compounds, each contributing to its health benefits. Here is an overview of its primary chemical constituents:

1. Alkamides

Alkamides are a group of fatty acid amides that are among the most prominent bioactive compounds in *E. purpurea*. These compounds, found primarily in the roots and aerial parts, have been shown to have immune-modulating properties. Alkamides are believed to interact with the endocannabinoid system and contribute to the plant's ability to stimulate the immune system, reduce inflammation, and combat microbial infections (22-25).

2. Caffeic Acid Derivatives

Caffeic acid derivatives are another significant group of compounds found in *E. purpurea*. Echinacoside, a major caffeic acid derivative, is frequently highlighted for its antioxidant and anti-inflammatory effects. These compounds help reduce oxidative stress and play an important role in immune function. Other phenolic compounds, such as chlorogenic acid and its derivatives, have also been identified and are believed to contribute to the plant’s therapeutic effects (26-29).

3. Flavonoids

Flavonoids, including rutin, quercetin, and nicotiflorin, are abundant in *E. purpurea* and exhibit significant antioxidant activity. Rutin, in particular, is well known for its anti-inflammatory properties and its ability to strengthen capillaries. These flavonoids have been shown to protect against oxidative damage, reduce inflammation, and support cardiovascular health (21, 30, 31).

4. Polysaccharides

Polysaccharides are complex carbohydrates that are particularly abundant in the roots of *E. purpurea*. These compounds are essential for immune function, as they stimulate the activity of white blood cells such as macrophages and neutrophils, which are crucial components of the body’s defense mechanisms. Polysaccharides contribute to the immunostimulatory properties of the plant by enhancing the body’s ability to fight infections (30, 32-34).

5. Glycoproteins

E. purpurea contains glycoproteins, which are proteins bound to carbohydrates. These compounds are involved in various biological activities, including enhancing immune responses and acting as anti-inflammatory agents. They may also contribute to the plant's ability to reduce allergic reactions and promote wound healing (35-38).

6. Polyacetylene

Polyacetylene compounds, which are a type of organic compound, have been identified in *E. purpurea* and are known for their antimicrobial properties. They may help the plant resist bacterial and fungal infections. While their concentration is lower compared to other compounds like alkamides, polyacetylenes contribute to the plant's overall therapeutic effects (39-42).

7. Essential Oils

The essential oils of *E. purpurea* contain a variety of volatile compounds, including sesquiterpenes, which possess anti-inflammatory and antimicrobial properties. These oils have been studied for their ability to alleviate symptoms of colds and respiratory infections, reinforcing the plant's use in traditional medicine (43-45).

8. Other Compounds

E. purpurea also contains sterols, fatty acids, and saponins. Sterols and fatty acids are involved in the plant's structural integrity and play a role in modulating inflammatory responses. Saponins, found in trace amounts, are known for their immune-boosting properties and have been studied for their potential antitumor activity (46-49).

In conclusion, the chemical composition of *E. purpurea* is diverse, with a rich array of compounds contributing to its well-known medicinal benefits. These compounds work synergistically to enhance immune function, reduce inflammation, fight infections, and provide antioxidant protection. Further research continues to explore how these chemicals interact and how they can be utilized in pharmaceutical and therapeutic applications.

Pharmacological Properties of *Echinacea purpurea*

The pharmacological effects of *E. purpurea* provide benefits in many areas, especially the immune system, thanks to its various biological activities. Studies on the pharmacological effects of *E. purpurea* reported in the literature are shown in Table 2.

Table (2): Pharmacological effects of *Echinacea purpurea*

Pharmacological Effects	Mechanism of Action	References
Immune System Stimulation Effects	Increases the activity of immune cells like macrophages, T-cells, and natural killer (NK) cells. Enhances cytokine production (IL-1, IL-6, TNF-α) which boosts immune responses.	(50, 51)
Antiviral Effects	Inhibits viral replication and prevents viral entry into host cells. Particularly effective in reducing the severity of common cold symptoms.	(52, 53)
Anti-inflammatory Effects	Modulates the NF-kB and MAPK pathways, balancing pro-inflammatory and anti-inflammatory cytokines, helping to reduce chronic inflammation.	(54, 55)
Antioxidant Effects	Contains flavonoids and caffeic acid derivatives that neutralize free radicals and protect immune cells from oxidative damage.	(25, 56)
Antibacterial Effects	Exhibits antibacterial properties, especially against respiratory pathogens, through the modulation of the immune response.	(45, 57)
Antifungal Effects	Some studies suggest that Echinacea purpurea may exhibit antifungal activity, especially against candida species.	(10, 58)

Immune System Stimulation Effects

The immune stimulating properties of *Echinacea purpurea* have been supported by various studies. One study revealed that *Echinacea* significantly increases immune cell activation. It has been shown that it particularly promotes the activation of macrophages and increases the production of cytokines such as IL-1, IL-6 and TNF-α, which play a critical role in the immune response (50). Similarly, a different study supports the effects of *Echinacea* on the immune system. This study emphasizes that *Echinacea* activates basic immune cells such as T cells and natural killer (NK) cells and contributes to immune defense against infections (51).

These findings demonstrate that *E. purpurea* exerts multifaceted effects on the immune system. Such studies highlight the potential of *Echinacea* to serve as a protective and supportive agent against infections, while also indicating its capacity to modulate immune responses. However, given the complex structure of the immune system, *Echinacea* should continue to be evaluated in clinical settings under standardized dosage and usage protocols. Additionally, the interactions of these effects with factors such as individual variability, disease type, and current immune status should be further investigated. In this context, supporting the mechanisms and clinical efficacy of *Echinacea*'s immunomodulatory effects through more comprehensive and controlled studies may play an important role in future therapeutic strategies.

Antiviral Effects

In a study on the antiviral properties of *Echinacea*, it was shown that *E. purpurea* extracts inhibited the replication of rhinovirus, a common cause of the common cold. The study suggested that *Echinacea* could reduce the severity of cold symptoms when administered early (53). In another study, *Echinacea* was found to reduce the duration of symptoms associated with upper respiratory tract infections (URIs). The findings suggested its potential to prevent the onset of viral infections and to shorten the course of illness (52).

Future studies should further investigate the effects of *Echinacea* against various pathogens, its molecular mechanisms, and its long-term safety. Additionally, the active constituents of the plant should be more clearly defined to ensure standardization in clinical applications. In this context, large-scale, controlled studies that account for individual variability will help clarify the plant's effects on the immune system.

Anti-inflammatory Effects

A study reported in the literature investigated the role of *E. purpurea* in the immune-enhancing effects of RAW264.7 cells and the underlying mechanisms of action. The study found that the plant extract significantly increased iNOS, COX-2, and mPGES-1 protein expression in RAW264.7 cells and increased

NO production, phagocytic activity, and cytokine expression. Consistent with these results, it was stated that phosphorylation of MAPKs (ERK, JNK, and p38) and NF-κB (IKKα/β, IκBα, and NF-κB p65) was induced after treatment (55). Another study reported in the literature evaluated the role of the complement system in the treatment of UC with Echinacea purpurea extract. The study observed that it reduced weight loss and diarrhea in rats with UC. It was also stated that it inhibited the level of proinflammatory cytokines and supported antioxidation. It has also been reported that the plant extract suppresses the expression of C3aR, CFB, CD55, TLR4 and NLRP3 (54). These studies reveal the immune system supporting and inflammation regulating effects of *E. purpurea*, highlighting its potential therapeutic role on both immune cell activation and inflammatory diseases. In particular, its effects on cellular signaling pathways provide an important perspective in understanding how the plant can modulate the immune response. However, how the effects of *Echinacea* on immunity and inflammation respond to different dosages, application times and interorganismal variability should be supported by more comprehensive studies. In particular, the results of long-term use on immune tolerance and possible adverse effects should be further investigated. In this context, data based on clinical studies are critical to clarify the therapeutic potential of the plant.

Antioxidant Activity Effects

Echinacea preparations are widely used as alternative therapy to prevent common cold and upper respiratory tract infections. In the literature, after extraction, fractionation and isolation, the antioxidant activity of three extracts from *E. purpurea* root, one alkamide fraction, four polysaccharide-containing fractions and three caffeic acid derivatives was evaluated by measuring the inhibition of in vitro Cu(II)-catalyzed oxidation of human low-density lipoprotein (LDL). The antioxidant activities of the isolated caffeic acid derivatives were compared with echinacoside, caffeic acid and rosmarinic acid for reference. The antioxidant activity of the tested substances was stated as cichoric acid > echinacoside ≥ derivative II ≥ caffeic acid ≥ rosmarinic acid > derivative I (56). A different study found that antioxidant compounds in *Echinacea* contribute to reducing oxidative damage in immune cells and support the body's defense mechanisms against pathogens (25).

These findings suggest that *E. purpurea* not only supports the immune system but also reduces cellular oxidative stress. It is thought that antioxidant components may contribute to the prevention of inflammation and chronic diseases by protecting immune cells from the harmful effects of free radicals. In particular, the lipid peroxidation inhibitory properties of these compounds suggest that they may have potential therapeutic value for conditions related to oxidative stress, such as cardiovascular diseases. However, further studies are required in different cellular and in vivo models to fully understand the antioxidant mechanisms of *Echinacea*. In addition, evaluation of factors such as bioavailability and metabolic stability of the bioactive components of the plant is critical to determine its clinical efficacy.

Antibacterial Effects

In a study reported in the literature, it was determined that the essential oil extract of *E. purpurea* obtained in antimicrobial activity property did not seem to be effective for *Staphylococcus aureus*, but it inhibited the growth of several bacterial species. In addition, it was stated that *E. purpurea* essential oil extract and its main components induced intracellular calcium mobilization in human neutrophils, and pretreatment of human neutrophils with the essential oil or (+)-δ-cadinene suppressed agonist-induced neutrophil calcium mobilization and chemotaxis. In addition, pharmacophore mapping studies predicted two potential MAPK targets for (+)-δ-cadinene. It was reported to be consistent with previous reports on the innate immunomodulatory activities of β-caryophyllene, α-phellandrene and germacrene D. Therefore, this study identified δ-cadinene as a novel neutrophil agonist and it was stated that δ-cadinene may contribute to the reported immunomodulatory activity of *E. purpurea* (45). Another study reported that a commercially standardized extract of *E. purpurea* (Echinaforce®) easily inactivated *Streptococcus pyogenes* (Group A Strep), which is usually associated with sore throat and more severe lung infections, *Hemophilus influenzae* and *Legionella pneumophila* were also easily inactivated, and *Taphylococcus aureus* (methicillin-resistant and susceptible strains) and *Mycobacterium smegmatis* were less susceptible to the bactericidal effects of *Echinacea* (57).

These studies suggest that the antibacterial and immunomodulatory effects of *E. purpurea* are not limited to direct effects against specific pathogens, but also operate through biological mechanisms that shape the host immune response. In particular, the effects of the plant's essential oil components on neutrophil activation suggest a potential role in regulating the innate immune system. However, the variability of bacterial susceptibility profiles suggests that the antibacterial activity of *Echinacea* may depend on specific microorganisms, chemical structure of the components, and application methods. Therefore, more comprehensive analyses at the component level should be performed to clarify its activity against different pathogen types and its potential for clinical use should be detailed.

Antifungal Effects

A study has shown that plant extracts containing acetylenic isobutylamides and polyacetylenes, previously reported to be present in *Echinacea*, have phototoxic antimicrobial activity against fungi, including clinically important pathogenic fungi. The results indicated that hexane extracts of *Echinacea* variably inhibited the growth of yeast strains of *Saccharomyces cerevisiae, Candida shehata, C. kefyr, C. albicans, C. steatulytica* and *C. tropicalis* under near-UV irradiation (phototoxicity) and to a lesser extent without irradiation (conventional antifungal activity) (58). These findings indicate that the antifungal effects of *E. purpurea* are not limited to direct microbial inhibition but may vary depending on environmental factors. In particular, the suppression of fungal growth through phototoxic mechanisms reveals how the biological activity of the plant can be modulated by external factors such as light. This suggests that *Echinacea* extracts can be evaluated as a potential agent in innovative antifungal strategies such as photodynamic therapy. However, further research is needed regarding the specific effects of this mechanism on cell damage, the limits of safe use and clinical applicability.

Mechanisms and Pathways

E. purpurea, commonly used in traditional medicine, is widely recognized for its immunostimulatory effects. The plant's active compounds, particularly alkamides, flavonoids, and polysaccharides, are believed to enhance immune system activity through several mechanisms.

Below are the key ways in which *E. purpurea* exerts its effects on the immune system:

Activation of Macrophages and Phagocytosis

One of the primary ways that *E. purpurea* boosts the immune system is by enhancing the activity of macrophages, which are key players in the innate immune system. The alkamides, especially, are thought to stimulate the activity of macrophages, increasing their ability to phagocytose (engulf and digest) pathogens such as bacteria and viruses. This heightened phagocytic activity contributes to the body's initial defense against infections (7, 59-61).

This mechanism suggests that *E. purpurea* supports the immune system not only directly against pathogens but also by optimizing the functions of host defense cells. Increased macrophage activity not only accelerates pathogen elimination through phagocytosis, but also increases the release of signaling molecules (cytokines) that activate other immune cells, contributing to the coordination of the immune response. This enables the immune system to mount a rapid and effective response, especially in the early stages of infections, while also highlighting the potential immunomodulatory role of *Echinacea*. However, the long-term effects of this effect on immune homeostasis and factors such as possible immune overactivation should be investigated in more detail.

Increase in Cytokine Production

E. purpurea has been shown to stimulate the production of cytokines, which are signaling molecules that play a crucial role in regulating immune responses. Specifically, studies have indicated that *Echinacea* can increase the production of pro-inflammatory cytokines such as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α). These cytokines are involved in activating various immune cells, such as T lymphocytes and neutrophils, enhancing the immune response to pathogens (62-65).

These findings suggest that the immunostimulatory effect of *E. purpurea* is not limited to specific cellular mechanisms, but also operates through signaling networks that contribute to the overall regulation of the immune response. While increasing the production of pro-inflammatory cytokines supports the establishment of an early and strong immune response against infections, this effect should be balanced in terms of the risk of excessive inflammation. It is important to evaluate the effects of *Echinacea* on immunity, especially in individuals with chronic inflammatory diseases or in cases where autoimmune responses are present, taking into account individual differences. Therefore, more clinical studies are required to determine its long-term effects on the immune system and optimal dose ranges.

Stimulation of T and B Cells

E. purpurea not only affects innate immunity but also stimulates adaptive immunity. Research suggests that the plant's compounds can increase the activity of T cells and B cells, which are crucial for recognizing and responding to specific pathogens. T cells play an important role in identifying infected cells, while B cells are responsible for producing antibodies that neutralize pathogens. This dual stimulation of both the innate and adaptive immune systems makes *Echinacea* a potent immune-enhancing herb (66-69).

These findings highlight the potential of *E. purpurea* to activate both major components of the immune system. The fact that it enhances both innate and adaptive immune responses suggests that the plant may play a multifaceted role in defending against infections. In particular, increasing the ability of T cells to recognize infected cells and B cells to produce antibodies allows the immune system to respond more specifically and effectively. This means that *Echinacea* could be a valuable supportive therapy, especially for individuals suffering from recurrent infections and immunodeficiency. However, further clinical studies are needed to understand the plant's long-term effects on adaptive immunity, as excessive immune activation could potentially lead to autoimmune diseases.

Inhibition of Viral Replication

Some studies suggest that *E. purpurea* may also inhibit the replication of viruses. This antiviral activity, likely mediated by the plant's phenolic compounds and alkamides, could help prevent or shorten the duration of viral infections such as the common cold. By interfering with the replication of viruses, *Echinacea* aids the body in mounting an effective defense against viral pathogens (70-72).

These findings suggest that *E. purpurea* may play a potential role in the prevention and treatment of viral infections. The ability of the plant's phenolic compounds and alkamides to inhibit viral replication may be beneficial in shortening the duration of common viral infections such as the common cold or preventing infection. However, further research into the mechanisms of this antiviral effect and how it works across a wide range of viruses is important. It is suggested that *Echinacea* may play a balancing role in targeting viruses to prevent overstimulation of the immune system and to ensure that viruses are effectively controlled.

Antioxidant Properties

The antioxidant compounds in *Echinacea*, such as flavonoids, caffeic acid derivatives, and echinacoside, help protect immune cells from oxidative stress. This protection is crucial because oxidative stress can damage immune cells, impairing their ability to function properly. By neutralizing free radicals, *Echinacea* helps maintain the health and effectiveness of immune cells during immune responses (73-75).

These findings highlight how *E. purpurea*'s ability to protect immune cells from oxidative stress is critical to healthy immune system function. Oxidative stress impairs immune cell function through free radical damage, which can weaken the body's defenses against infection. The antioxidant compounds in *Echinacea* neutralize free radicals, allowing immune cells to function efficiently. This may be important for maintaining cell health and preventing potential tissue damage, especially during periods of infection when the immune response is intense. However, further research on how antioxidant activity regulates immune response and what its long-term effects may be is important to fully evaluate the therapeutic potential of this plant.

Regulation of Inflammatory Pathways

E. purpurea has been shown to regulate inflammatory pathways, specifically the NF-kB pathway, which is involved in the transcription of pro-inflammatory genes. By modulating this pathway, *Echinacea* helps balance the immune system's response to infections and prevents excessive inflammation that can lead to tissue damage (54, 76, 77).

These findings suggest that *E. purpurea* plays a balancing role in the immune response and contributes to the prevention of excessive inflammation. Modulation of the NF-kB pathway highlights the ability of this plant to regulate inflammatory

processes, as this pathway triggers immune cells to produce pro-inflammatory cytokines and other immune response molecules. By balancing this pathway, *Echinacea* provides a strong response to infections but prevents excessive inflammation from causing tissue damage. This suggests potential benefits, particularly in conditions associated with chronic inflammation and autoimmune diseases. However, further research is needed to fully understand the clinical implications of this mechanism, as long-term effects and the impact of dosage are important.

Clinical Findings

Clinical research on *E. purpurea* suggests its potential to enhance immune responses in various ways. For instance, several trials have demonstrated that Echinacea supplementation can shorten the duration and severity of cold and flu symptoms, especially when administered early. Additionally, *Echinacea* has been shown to enhance post-vaccination antibody production, suggesting an immune-priming effect. Furthermore, routine use of *Echinacea* may lower the risk of developing upper respiratory tract infections, as supported by multiple controlled studies (51, 78, 79)

E. purpurea, commonly known for its immune-enhancing properties, has been the subject of numerous clinical studies aimed at understanding its role in modulating the immune system. These studies have provided valuable insights into how *Echinacea* affects immune responses, particularly in terms of respiratory infections and overall immune function. A significant amount of research has demonstrated that *E. purpurea* enhances the activity of key immune cells, including macrophages, natural killer (NK) cells, and T-cells. These cells play critical roles in defending the body against pathogens. For instance, studies have shown that *Echinacea* stimulates macrophages, which are involved in pathogen recognition and elimination. The activation of these immune cells is essential for initiating an effective immune response, especially during infections such as the common cold and influenza. Clinical trials also highlight *Echinacea*'s ability to increase the production of cytokines, which are signaling molecules that regulate immune responses. Notably, *Echinacea* can modulate both pro-inflammatory and anti-inflammatory cytokines, helping to balance the immune system's reaction to infections. This cytokine modulation is key to preventing excessive inflammation while still promoting an effective immune defense. The efficacy of *Echinacea* in preventing or reducing the severity of upper respiratory tract infections has been explored in several randomized, double-blind, placebo-controlled trials. Results from these studies generally suggest that *Echinacea* can reduce the severity and duration of symptoms associated with colds, although some studies report mixed results regarding its overall effectiveness. This variability can be attributed to differences in study design, the form of *Echinacea* used (such as extracts or teas), and the quality control of the preparations. Moreover, ongoing studies continue to investigate the molecular mechanisms through which *Echinacea* influences immune pathways. Research into signaling pathways like NF-κB and MAPK, which regulate immune cell activation and cytokine production, has shown that *Echinacea* interacts with these pathways to enhance immune function. Despite these promising findings, there is a need for more rigorous and large-scale trials to confirm the optimal dosage, formulation, and long-term safety of *Echinacea* as a therapeutic agent for immune support. Overall, while evidence supports the role of *Echinacea* in boosting immune function, further clinical studies are essential to clarify the best practices for its use, as well as its potential interactions with other therapies (54, 76, 77, 80-83).

Side Effects and Restrictions

E. purpurea, although widely used for its immune-boosting properties, may cause some side effects, especially when used improperly or in sensitive individuals. While it is generally considered safe for short-term use, prolonged use or excessive dosages may lead to adverse reactions.

Here are some potential side effects associated with *E. purpurea*:

Allergic Reactions

One of the most common side effects of *E. purpurea* is allergic reactions, especially in individuals who are allergic to plants in the Asteraceae family (such as ragweed, chrysanthemums, or marigolds). Symptoms of an allergic reaction can include skin rashes, swelling, itching, and difficulty breathing. In severe cases, an allergic reaction may result in anaphylaxis, a potentially life-threatening condition (15, 17, 84).

These findings emphasize that although *E. purpurea* has strong effects on the immune system, it should be used with caution, especially in individuals who are allergic to plants belonging to the Asteraceae family. Allergic reactions can trigger an overreaction of the immune system due to the immune modulatory properties of the plant. This requires that individual sensitivities and existing allergic tendencies be taken into account, especially when using immune-stimulating plants. In order to reduce the risk of serious reactions such as anaphylaxis, it is important to perform allergy tests and seek medical advice before using *Echinacea*. In addition, it can be said that *Echinacea* should be used with caution in terms of dosage and duration of use in order to prevent such side effects.

Gastrointestinal Issues

Some individuals may experience gastrointestinal discomfort when using *Echinacea*, including symptoms such as nausea, stomach cramps, or diarrhea. These side effects are typically mild and resolve after discontinuing the herb, but individuals with sensitive digestive systems may need to avoid it or consult a healthcare provider before use (15, 85).

These findings suggest that *E. purpurea* may cause mild digestive discomfort in some individuals. In particular, complaints such as nausea, cramps, or diarrhea may be due to the plant's stimulating effects on the stomach and intestines. Such side effects usually improve temporarily when use is stopped, but may become more pronounced in individuals with sensitive digestive systems. It is important for those with digestive problems to consult their health care professional before using *Echinacea*, as the effects of the plant can vary from person to person. It should also be noted that these side effects are rare and can usually be minimized by adjusting the dosage.

Immune System Overactivation

Echinacea stimulates the immune system, which can be beneficial for combating infections. However, in individuals with autoimmune conditions (such as lupus, rheumatoid arthritis, or multiple sclerosis), this stimulation could potentially exacerbate the disease. It is important for individuals with autoimmune disorders to consult their healthcare provider before using *Echinacea* (84, 86).

These findings emphasize that the immunostimulatory effects of Echinacea purpurea require careful use in individuals

with autoimmune diseases, where the immune system is overactive. When the immune system is stimulated, this can worsen the symptoms of existing autoimmune diseases or accelerate the course of the disease. In particular, diseases such as lupus, rheumatoid arthritis or multiple sclerosis, where the immune system is triggered to fight against the body, may have negative effects on these diseases. Therefore, it is very important for individuals with autoimmune diseases to consult their doctors before using *Echinacea* in order to prevent possible negative effects during the treatment process.

Interaction with Medications

Echinacea may interact with certain medications, particularly immunosuppressive drugs (like corticosteroids) and drugs that affect liver enzymes (such as cytochrome P450). The herb's immune-stimulating properties may interfere with medications designed to suppress immune function. Additionally, *Echinacea* may alter the metabolism of certain drugs, potentially increasing or decreasing their effectiveness (87-89).

These findings suggest that *E. purpurea* may interact with certain medications, and these interactions may affect the treatment process. Especially when used with immunosuppressive drugs and drugs that affect liver enzymes, *Echinacea*'s immune-stimulating properties may alter the effectiveness of the drugs. For example, when used with immunosuppressive drugs such as corticosteroids, *Echinacea* may lead to overstimulation of the immune system, which may have an adverse effect on the treatment. In addition, since the plant may affect the metabolism of certain drugs and change how the drugs are processed in the body, the effectiveness or side effects of the drugs may also be altered. In order to avoid such interactions, it is very important to seek medical guidance to evaluate possible interactions between *Echinacea* use and drug therapy.

Potential Liver Toxicity

Although rare, some reports suggest that prolonged use of high doses of *Echinacea* could potentially contribute to liver toxicity. Individuals with pre-existing liver conditions or those using other hepatotoxic drugs should exercise caution and consult a healthcare provider before using *Echinacea* (84, 90).

These findings suggest that long-term and high-dose use of *E. purpurea* can rarely lead to liver toxicity. The liver is one of the main organs that detoxify toxins in the body and can be damaged if overloaded. It is thought that *Echinacea* may increase this risk, especially in individuals with liver disease or those using hepatotoxic drugs. Therefore, it is important to consult a health care professional before using *Echinacea* in cases where liver health should be taken into consideration. In addition, more clinical studies are needed to better understand the potential toxic effects of the plant.

Skin Reactions

Some individuals may experience skin irritation or reactions after using topical forms of *Echinacea*, such as creams or ointments. These reactions may include redness, itching, or a rash. It is advisable to perform a patch test on a small area of skin before applying *Echinacea* products topically (84, 91).

These findings suggest that topical use of *E. purpurea* may cause skin irritation or allergic reactions in some individuals. Reactions, particularly redness, itching or rash, may occur in individuals who are sensitive to the plant's components. Therefore, before using topical *Echinacea* products, it is useful to perform a patch test on a small area to avoid possible skin reactions. Such reactions are usually temporary and resolve when the product is stopped. However, it is important for individuals with skin sensitivities to exercise caution and seek dermatological advice if necessary.

Conclusion and Future perspective

Studies on *Echinacea* (*E. purpurea*) show that this plant provides immune system support, antiviral, antioxidant and anti-inflammatory effects. The polysaccharides, alkamides, flavonoids and phenolic compounds it contains activate immune cells and strengthen body defenses. It has also been determined that echinacea can reduce the duration and severity of respiratory tract infections and play a protective role against chronic diseases by regulating inflammatory processes. However, some issues regarding the effectiveness and safety of echinacea are still unclear. Factors such as long-term use, dosage differences and individual immune responses should be investigated further. Potential risks such as overstimulation of the immune system, especially in individuals with autoimmune diseases, should be taken into consideration. It is of great importance for future studies to determine the most effective methods of use by comparing the pharmacological effects of different types and extracts of echinacea. In addition, more comprehensive and controlled clinical studies should be conducted on the bioavailability, clinical efficacy and long-term safety of echinacea. Such research could contribute to a more widespread and safe use of echinacea in modern medicine, making it an important herbal agent that supports the immune system. Furthermore, future research integrating molecular docking and in silico simulations may offer deeper insights into the target-specific interactions of *Echinacea* phytoconstituents.

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