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REVIEW

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Echinacea purpurea: An overview of mechanism, efficacy, and safety in pediatric upper respiratory infections and otitis media

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ABSTRACT

Pediatric upper respiratory infections (URIs) and otitis media (OM) significantly impact the health of children globally. *Echinacea purpurea*, known for its immunomodulatory, anti-inflammatory, and antimicrobial properties, has been historically used to treat various ailments, suggesting its potential as an adjunctive treatment in pediatric respiratory conditions. This narrative review synthesizes literature from January 2000 to December 2023 on the efficacy and safety of *E. purpurea* in treating pediatric URIs, including OM. It focuses on clinical trials and empirical studies that explore the mechanisms of action, such as the modulation of cytokine production, inhibition of NF-κB signaling, and antimicrobial effects. The analysis reveals mixed outcomes regarding the efficacy of *E. purpurea* in pediatric populations, attributed partly to variability in study designs and lack of standardized treatment protocols. While some studies report reduced severity and duration of respiratory symptoms, others indicate minimal or no significant difference compared to placebo. The review also highlights the need for specifically designed products that cater to the unique physiological and metabolic needs of children. Rigorous, well-designed clinical trials are crucial for establishing clear guidelines on the use of *E. purpurea* in pediatric respiratory care, ensuring its safe and effective application in improving health outcomes for children.

1. Introduction

Upper respiratory infections (URIs) represent a significant health concern in pediatric populations, manifesting as a leading cause of acute illness and a primary reason for visits to healthcare providers worldwide. The incidence of URIs is notably elevated among preschool-aged children owing to their evolving immune systems and heightened exposure to pathogens in daycare or educational environments (Jin et al., 2021; Kusel et al., 2007; Ostrzyżek-Przeździecka et al., 2023). These infections, characterized by symptoms such as cough, fever, and sore throat, can significantly impact a child's well-being and development (Ogal et al., 2021; Ren et al., 2019). Common causative agents among pediatric cases include various viruses such as rhinovirus, influenza virus, respiratory syncytial virus (RSV), adenovirus, and coronaviruses. Additionally, bacterial pathogens like *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis* may contribute to URIs, particularly in instances of secondary bacterial in-

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fection (Bellussi et al., 2019; van Doorn & Yu, 2020). URIs, including nasopharyngitis, pharyngitis, and tonsillitis, and complications such as otitis media (OM), account for 87.5% of all respiratory tract infections (Nguyen-Van-Tam et al., 2022). OM, a common complication of URIs, often manifests following these infections, illustrating a direct clinical linkage (Durmaz et al., 2021; Principi & Esposito, 2020). OM is predominantly caused by bacteria like *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*, with viruses also playing a role (Folino et al., 2022; Zahid et al., 2024).

OM is bifurcated into acute OM, with distinct symptoms, and OM with effusion, marked by fluid retention without symptoms (Jamal et al., 2022; Spoială et al., 2021). Notably, acute OM affects a significant portion of children with viral URIs. The management of OM often involves extensive antibiotic therapy and surgical interventions on the ear, constituting a significant component of pediatric healthcare expenditures (Spoială et al., 2021). These conditions significantly contribute to the burden of illness, healthcare utilization, and economic costs. Despite advancements in medical management, treating pediatric URI and OM remains a clinical challenge, prompting the exploration of alternative and complementary therapeutic approaches.

In the treatment and prevention of URIs and OM, a broad spectrum of drugs are employed. For URIs, antiviral medications such as oseltamivir and zanamivir are commonly used to treat influenza, while antibiotics like amoxicillin and azithromycin are prescribed for bacterial infections (Nitsch-Osuch et al., 2016). In cases of OM, amoxicillin is typically the first-line treatment, with alternatives such as amoxicillin-clavulanate, cefdinir, and cefuroxime used when resistance or allergies are a concern (Dawit et al., 2021). In addition to pharmaceutical interventions, several species of plants, including *Echinacea purpurea*, have been explored for their therapeutic benefits.

E. purpurea, commonly known as purple coneflower, is a flowering plant native to North America with a long history of traditional medicinal use (Figure 1). The plant has been used for centuries by indigenous peoples and later adopted by European settlers for its purported therapeutic properties, particularly in the treatment of respiratory infections, wounds, and immune-related conditions. *E. purpurea* is rich in bioactive compounds, including alkamides, polysaccharides, flavonoids, and phenolic acids, which are believed to contribute to its immunomodulatory, anti-inflammatory, and antimicrobial effects (Balčiūnaitė-Murzienė et al., 2021; Burlou-Nagy et al., 2022; Daley, 2019).

Figure 1. *E. purpurea* plant parts
(A. root, B. stem, C. flower, D. Fruit)

With the rise in pediatric URIs, scientists have increased the discovery of herbal medicines to improve treatment effectiveness. Currently, *E. purpurea* is widely used across various global regions as an over-the-counter remedy for URIs and OM due to its reported immunomodulatory properties. The rationale for studying *E. purpurea* in pediatric URI and OM lies in its immune-modulating, anti-inflammatory, and antimicrobial properties, which may offer potential benefits in reducing symptom severity, duration of illness, and recurrence rates in affected children.

2. Methodology

This study employed a narrative review methodology, as previously described (Snyder, 2019). This review synthesized research findings from studies published from January 2000 to December 2023, providing an overview of the efficacy and safety of *E. purpurea* in pediatric respiratory conditions. The review specifically focused on the exploration of mechanisms of action, such as immunomodulatory, anti-inflammatory, and antimicrobial effects. A structured approach was used to search the literature, employing keywords like '*E. purpurea*', 'pediatric respiratory infections', 'children URI treatment', and '*Echinacea* safety in children', using AND/OR operators to refine the search results. Inclusion criteria were studies that investigated the clinical efficacy and safety of *E. purpurea* in children, with a focus on randomized controlled trials, observational studies, and empirical research. Exclusion criteria included studies lacking sufficient data on outcomes or those focusing on adult populations. Data extraction targeted information on the age range of participants, treatment duration, outcomes measured (i.e. efficacy and safety), and key findings.

3. Empirical use of *E. purpurea*

3.1. Historical values of E. purpurea

E. purpurea, belonging to the Asteraceae family, has been historically valued in indigenous medicine for its healing properties and has gained popularity in modern complementary medicine, particularly for immune system support and as a remedy for colds and respiratory infections. Indigenous peoples of North America, such as the Plains Indians, historically used *E. purpurea* for its medicinal properties to treat various ailments, including respiratory infections, wounds, and snake bites (Aarland et al., 2017; Oláh et al., 2017; Pires et al., 2016). European settlers adopted the use of *E. purpurea* from Native American traditions, leading to its incorporation into Western herbal medicine practices in the late 19th century. *E. purpurea* has been prepared for use as a topical treatment for skin and wound inflammation and is currently licensed in Europe for treating infections of the upper respiratory tract and for wound healing (Burlou-Nagy et al., 2022; Kilani-Jaziri et al., 2017; Ogal et al., 2021; Sharifi-Rad et al., 2018; Thomsen et al., 2018). In modern clinical practice, *E. purpurea* is utilized for its immunomodulatory, anti-inflammatory, and antimicrobial properties, making it a popular over-the-counter remedy for URIs and OM. The bioactive compounds in *E. purpurea*, such as alkamides, polysaccharides, flavonoids, and phenolic acids, are believed to contribute to its therapeutic effects (Balčiūnaitė-Murzienė et al., 2021; Burlou-Nagy et al., 2022; Daley, 2019).

3.2. Phytochemical profile of E. purpurea

The plant is rich in phytochemicals such as alkamides, glycoproteins, polysaccharides, and flavonoids, which are believed to contribute to its therapeutic effects (Truong et al., 2023). These compounds are thought to enhance immune function, offering anti-inflammatory, antiviral, and antioxidant benefits. Potential mechanisms of *E. purpurea* include modulation of cytokine production and enhancement of leukocyte activity, which may help mitigate the symptoms and duration of URI. Its widespread use in alternative medicine prompts the need for continued research, into its efficacy and safety, particularly in vulnerable populations such as children.

E. purpurea contains a complex mixture of bioactive compounds, including alkamides, caffeic acid derivatives, polysaccharides, flavonoids, and essential oils (Daley, 2019; Dosoky et al., 2023; Xu et al., 2021). The main chemical composition of *E. purpurea*, as reported by previous studies (Burlou-Nagy et al., 2022), is outlined in Table 1. These chemical constituents are of significant importance in both botanical and pharmaceutical research, as they underlie the potential therapeutic properties associated with *E. purpurea*. The chemical composition of *E. purpurea* is characterized by a wide range of bioactive compounds distributed across different plant parts. The root, with its alkamides and glycoproteins, appears to be a particularly valuable source of bioactive compounds (Petrova et al., 2023). Additionally, the presence of polysaccharides, caffeic acid derivatives, and volatile oils in various plant parts prompts the complexity of the chemical.

Table 1. Summary of chemical components and their pharmacological effects in some parts of *E. purpurea*

Chemical components	Plant part	Pharmacological effects	References
Alkamides	Root, aerial part	Immunomodulatory, anti-inflammatory, antimicrobial, anticancer, antiviral, antifungal, analgesic, antioxidant, antidiabetic	(Aarland et al., 2017; Balciunaite et al., 2020; Burlou-Nagy et al., 2023; Manayi et al., 2015; Miller & Yu, 2004; Petkova et al., 2023)
Polysaccharide: Pectin-like polysaccharide	Root, aerial part	Immunomodulatory, anti-inflammatory, antidiabetic, antioxidant, antimicrobial, anticancer, antifungal, antiviral, gastrointestinal protective, hypoglycemic, hepatoprotective	(Burlou-Nagy et al., 2023; Hou et al., 2020; Jiang et al., 2021; Manayi et al., 2015; Petrova et al., 2023; Ren et al., 2023; Xu et al., 2021)
Caffeic acid derivatives: Chicoric acid, caftari acid	Root, aerial part	Immunomodulatory, anti-inflammatory, antioxidant, antimicrobial, anti-tumoral, antiosteoporotic, neuroprotective action	(Adebimpe Ojo et al., 2024; Ávila-Gálvez et al., 2024; Manayi et al., 2015; Miller & Yu, 2004; Petrova et al., 2023; Tsai et al., 2012)
Glycoprotein	Root	Immunomodulatory	(Adebimpe Ojo et al., 2024; Balciunaite et al., 2020)
Flavonoids: Luteolin, rutosid, nicotiflorin, rutin	Leaves	Anti-inflammatory, antiallergic, antioxidant, antiviral	(Burlou-Nagy et al., 2023; Kurkin et al., 2011; Lee et al., 2010; Maleki et al., 2019; Manayi et al., 2015)
Alkaloids: Tussilagin, isotussilagin	Root, aerial part	Gastrointestinal-protective, anti-tumoral, hepatoprotective	(Aarland et al., 2017; Burlou-Nagy et al., 2023; Manayi et al., 2015; Miller & Yu, 2004; Petrova et al., 2023; Xu et al., 2021)
Volatile constituents: germacrene D, α-phellandrene, β-caryophyllene, γ-curcumene, α-pinene, δ-cadinene, α-cadinol	Root, leaves, flower	Antimicrobial, analgesic, anti-inflammatory, immunomodulatory	(Dosoky et al., 2023; Nyalambisa et al., 2017)

4. Potential mechanisms of action of *E. purpurea* on treating URI and OM

Research suggests that the bioactive constituents of *E. purpurea* exert immunomodulatory, anti-inflammatory, and antimicrobial effects, which contribute to its therapeutic properties in treating respiratory infections (Dobrange et al., 2019). The potential mechanisms of action and the rationale for studying *E. purpurea* in the context of URIs and OM include:

4.1. Immune-modulating

E. purpurea contains a diverse array of bioactive compounds, including alkamides, caffeic acid derivatives, polysaccharides, and glycoproteins, which are believed to underlie its immunostimulatory properties (Awortwe et al., 2021; Balciunaite et al., 2020; de Oliveira et al., 2021; Ren et al., 2023; Vieira et al., 2023). These ingredients have been shown to have the ability to activate both cellular and humoral immunity by increasing the production and activation of white blood cells, lymphocytes, monocytes, and cytokines (Declerck et al., 2021; Khalaf et al., 2019).

Previous studies have shown that *E. purpurea* can modulate interferon signaling and silence endogenous retroviral sequences through DNA hypermethylation in monocytes, highlighting its potential to boost innate and adaptive immunity, crucial for combating respiratory infections in pediatric populations (Declerck et al., 2021). Clinical evidence supports this potential. Cohen et al. (2004) found that *E. purpurea* reduced the incidence and duration of URIs in children aged 1 to 5 years, while Weber et al. (2005) reported a decreased risk of subsequent URIs in children using *E. purpurea*. Additionally, Wahl et al. (2008) observed that *E. purpurea*

could reduce the frequency of OM episodes over six months, indicating its role in mitigating complications associated with URIs and OM in pediatric patients. A recent study found that *E. purpurea* significantly reduced the incidence and duration of URTIs and their complications, including otitis media, in children aged 4-12 (Ogal et al., 2021). These findings suggest the importance of further research to establish optimal dosage and administration guidelines for *E. purpurea* in treating pediatric respiratory infections.

E. purpurea has been shown to enhance immune function through multiple pathways, including the activation of white blood cells, lymphocytes, and cytokines. Recent studies, have demonstrated that *E. purpurea* can modulate interferon signaling and silencing of endogenous retroviral sequences through DNA hypermethylation in monocytes (Declerck et al., 2021). These mechanisms highlight the potential of *E. purpurea* in boosting innate and adaptive immunity, which is crucial for combating respiratory infections in pediatric populations

An increasing amount of research indicates that *E. purpurea* possesses immunostimulatory characteristics. *E. purpurea* boosts the immune system through three mechanisms: enhancing phagocytosis, stimulating fibroblasts, and promoting respiratory movement. These actions enhance the motility of white blood cells. Additionally, *E. purpurea* enhances immune function by increasing the quantity, functionality, and mobility of various immune cells, such as neutrophils, polymorphonuclear leukocytes, and natural killer (NK) cells, thereby augmenting innate immunity and exerting anti-inflammatory effects (Khattab et al., 2019; Paulovičová et al., 2022). For instance, *E. purpurea* root extract was found to enhance the immune system by reducing the frequency and function of regulatory T cells (Kim et al., 2012). In a separate study, oral administration of an *E. purpurea* extract boosted natural killer cell activity in mice by elevating the levels of MHC II, CD4 T cells, and Th1 cytokines (Park et al., 2021). Similarly, an ethanolic extract of the aerial parts was observed to regulate cytokine responses in human T-cells (Fonseca et al., 2014). The study conducted by Dosoky et al. (2023) demonstrated that the essential oils of *E. purpurea* and its major components exhibited microbicidal properties, while also exerting immunomodulatory effects on neutrophil activation.

Additionally, alkamides have shown efficacy against the cannabinoid receptor type 2 (CB2), suggesting a role in immune regulation through structural similarities with endogenous ligands (Woelkart & Bauer, 2007). The immunomodulatory effects of alkamides are driven by several signaling pathways. These include adenosine cyclic monophosphate (cAMP), p38 mitogen-activated protein kinase (p38/MAPK), and c-Jun N-terminal kinase (JNK). Other pathways involved are nuclear factor kappa light chain of activated B cells (NF-κB) and activating transcription factor cAMP response element binding protein 1 (ATF-2/CREB-1). These mechanisms occur in primary human macrophages and monocytes (Hohmann et al., 2011). A study by Declerck et al. (2021) revealed that phytochemicals derived from *E. purpurea* enhance antiviral innate immunity by regulating tonic interferon (IFN) levels, modulating pattern recognition and chemokine gene expression, and silencing human endogenous retroviruses (HERVs) through DNA repeat hypermethylation in monocytes. Moreover, polysaccharide extracts from *E. purpurea* roots and aerial parts have been reported to modulate the expression of insulin-like growth factor receptor (IGF1R) and certain genes related to immune cell function or activation. Conversely, aboveground parts of the plant, excluding flowers, have been observed to affect immune cell function negatively (Wang et al., 2006). The immunomodulatory properties of *E. purpurea* are particularly pertinent to pediatric URIs and OM, as effective immune responses are crucial for combating pathogens and minimizing tissue damage (Manayi et al., 2015). By enhancing both innate and adaptive immune defenses, *E. purpurea* may alleviate respiratory symptoms, prevent secondary infections, and expedite recovery in pediatric patients.

Furthermore, *E. purpurea* extracts have been found to stimulate mucosal immunity and reinforce the epithelial barrier function in the respiratory mucosa (Meeran et al., 2021). Through activation of immune cells such as dendritic cells and lymphocytes, *E. purpurea* enhances the secretion of mucosal immunoglobulins, strengthening the body's defense against respiratory pathogens (Balčiūnaitė-Murzienė et al., 2021; Declerck et al., 2021; Kim et al., 2021). Additionally, *E. purpurea* upregulates the expression of tight junction proteins and mucins in the respiratory epithelium, thereby maintaining the integrity of the epithelial barrier and preventing pathogen infiltration (Schoop, 2020). Mechanism of action for immune-modulating effects of *E. purpurea*, that may decrease the symptoms of URI and OM was proposed in Figure 2.

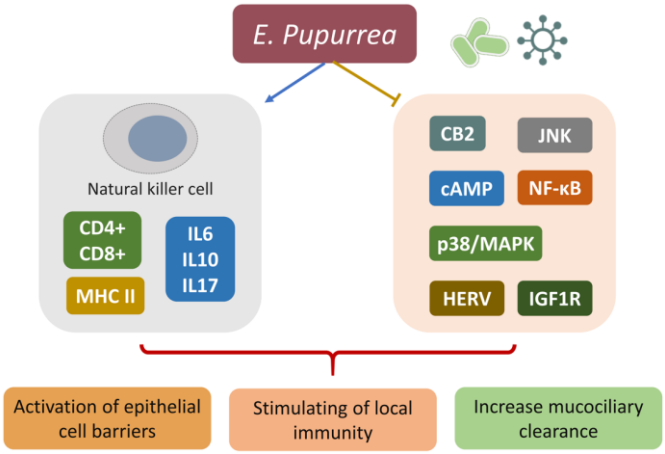

Figure 2. Proposed mechanism of action for immune-modulating effects of *E. purpurea*

4.2. Anti-inflammatory

Inflammation plays a crucial role in sustaining and safeguarding human health (Furman et al., 2019). However, excessive inflammation plays a central role in the pathogenesis of pediatric URIs and otitis media, contributing to tissue damage, symptom severity, and disease progression. Many studies have shown that alkamides, sesquiterpenes, polysaccharides, and caffeic acid derivatives are present in roots and aerial parts of *E. purpurea* exhibits anti-inflammatory effects (Burlou-Nagy et al., 2022; Cheng et al., 2020; Hou et al., 2020; Jiang et al., 2021; Kakouri et al., 2024; Li et al., 2020; Zhang et al., 2020).

The anti-inflammatory mechanism of the active compounds in *E. purpurea* is believed to be through inhibition of nuclear factor-kappa B (NF-κB) signaling, suppression of prostaglandin synthesis, and modulation of cyclooxygenase-2 (COX-2) expression. Studies have shown that alkylamides present in *E. purpurea* exhibit their anti-inflammatory effects by inhibiting the phosphorylation of p38, ERK 1/2, STAT 3, and/or NF-κB signaling pathways, and/or by reducing the expression of cyclooxygenase 2 (Vieira et al., 2023; Vieira et al., 2022). Other research conducted by Cheng et al. (2020) indicated that sesquiterpenes derived from *E. purpurea* demonstrate potent anti-inflammatory properties by inhibiting nitric oxide (NO) production in lipopolysaccharide (LPS)-induced RAW246.7 macrophages through the NF-κB signaling pathway.

Polysaccharides, predominant constituents found in medicinal plants, hold significant relevance in various essential biological functions, notably exhibiting anti-inflammatory properties (Batista et al., 2020; Huang et al., 2019; Sun et al., 2019; Wang et al., 2019). Research conducted by Zhang et al. (2020) demonstrated that *E. purpurea* mitigates lung injury induced by lipopolysaccharide (LPS) through the inhibition of inflammation, apoptosis, and the activation of the Toll-like receptor 4 (TLR4)/NF-κB signaling pathway. Multiple research investigations have indicated that among the phenolic compounds present in *E. purpurea*, caffeic acid derivatives, notably chicoric, caftaric, and chlorogenic acids, serve as principal bioactive components with anti-inflammatory properties. These compounds operate by mechanisms that decrease the synthesis of inflammatory mediators such as cytokines, reactive oxygen species (ROS), nitric oxide, TNF-α, and IL-1β (Vieira et al., 2023; Vieira et al., 2022).

By attenuating the release of pro-inflammatory cytokines and chemokines, *E. purpurea* may mitigate inflammation-induced mucosal injury, nasal congestion, and ear pain in pediatric patients with URI and OM. Mechanism of action for anti-inflammatory effects of *E. purpurea* may reduce the symptoms of URI and OM was proposed in Figure 3.

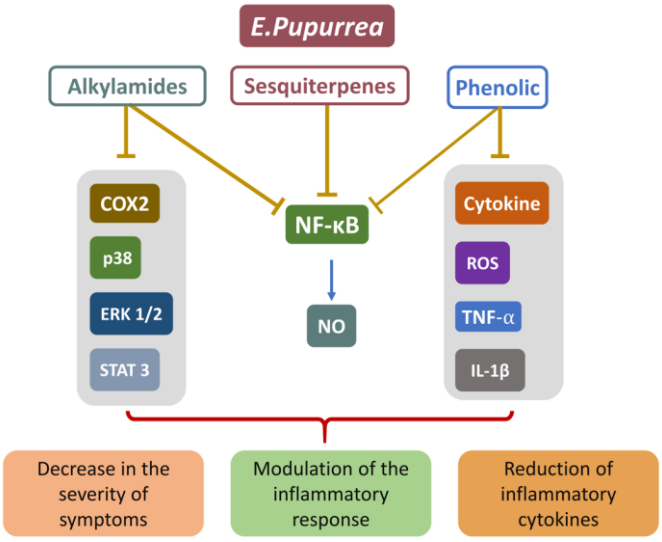

Figure 3. Proposed mechanism of action for anti-inflammatory effects of *E. purpurea*

4.3. Antiviral and antimicrobial

Conventional treatments for pediatric URIs and OM primarily focus on symptomatic relief and, in the case of bacterial infections, antibiotic therapy. However, concerns regarding antibiotic overuse, antimicrobial resistance, and adverse effects suggest the need for alternative, non-pharmacological interventions that are safe, effective, and well-tolerated in children (Basa & Sovtić, 2022; Marchisio et al., 2019).

E. purpurea represents a promising complementary therapy with the potential to reduce reliance on antibiotics, mitigate treatment-related adverse effects, and provide additional options for managing pediatric respiratory infections in a holistic and integrative manner. In addition to its immunomodulatory and anti-inflammatory properties, *E. purpurea* exhibits direct antimicrobial activity against both viral and bacterial pathogens implicated in pediatric respiratory infections. The chemical constituents responsible for the antimicrobial properties of *E. purpurea* encompass alkamides (Burlou-Nagy et al., 2022; Dobrange et al., 2019; Petkova et al., 2023), essential oils (Askari et al., 2020; Dosoky et al., 2023), polysaccharides, and caffeic acid derivatives. Alkylamides and caffeic acid derivatives found in *E. purpurea* extracts have been shown to inhibit viral replication and attachment, particularly against respiratory syncytial virus (RSV), influenza virus, and rhinovirus. Moreover, *E. purpurea* constituents possess antibacterial effects by disrupting bacterial cell membrane integrity, inhibiting biofilm formation, and interfering with bacterial quorum sensing, thus potentially reducing the risk of secondary bacterial complications in pediatric URI and OM. Additionally, in vitro experiments have shown direct antiviral and antibacterial activity of *E. purpurea* constituents against common pathogens implicated in pediatric URIs and otitis

media. The mechanism of action for the antibacterial effects of *E. purpurea*, possibly related to URI and OM was proposed in Figure 4.

4.4. Reduce the severity and duration of symptoms

Shortening the duration of illness and reducing symptom burden can enhance the quality of life for pediatric patients and their caregivers, as well as potentially decrease healthcare resource utilization and absenteeism from school or daycare (Venekamp et al., 2020). Clinical and preclinical evidence suggests that *E. purpurea* may have therapeutic benefits in alleviating symptoms associated with URI and OM (Burlou-Nagy et al., 2022). *E. purpurea* holds promise in reducing the severity and duration of symptoms, thereby improving patient outcomes and reducing healthcare burden. The mechanism of action of *E. purpurea* affecting the immune system, anti-inflammatory and antibacterial effects, leading to the reduction of symptoms related to URI and OM was proposed in Figure 5.

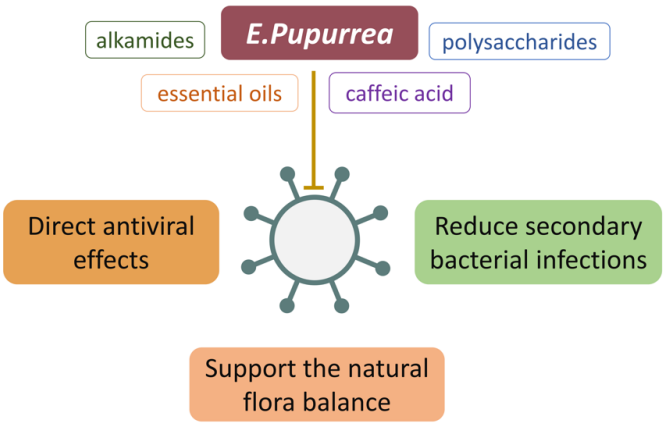

Figure 4. Proposed mechanism of action for antibacterial effects of *E. purpurea*

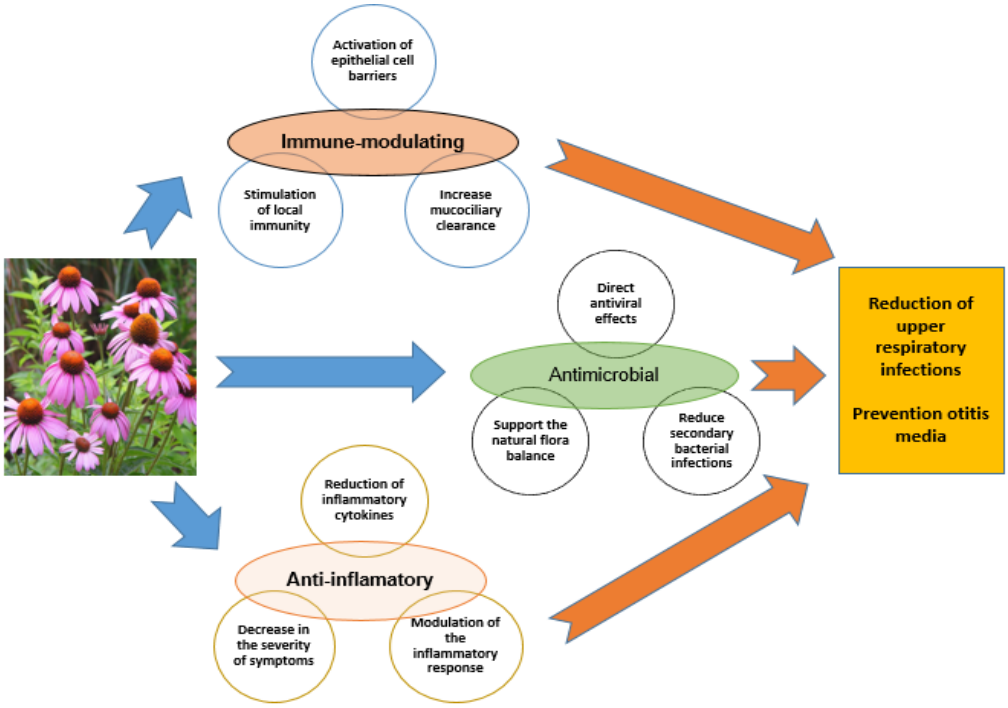

Figure 5. Mechanism of action of *E. purpurea* affecting the immune system, anti-inflammatory and antibacterial effects

Several studies have demonstrated the efficacy of *E. purpurea* in reducing the duration and severity of URI in pediatric populations (Aucoin et al., 2020; Weishaupt et al., 2020) (Table 2). By enhancing innate and adaptive immune responses, *E. purpurea* can help combat viral and bacterial pathogens, leading to faster recovery times and reduced symptom severity (Declerck et al., 2021; Weishaupt et al., 2020). Additionally, its anti-inflammatory properties may alleviate symptoms such as nasal congestion, sore throat, and coughing, further enhancing the patient's comfort and well-being (Meeran et al., 2021). Moreover, *E. purpurea* has shown potential in reducing the incidence and severity of otitis media, a common complication of URIs in children (Basa & Sovtić, 2022; Venekamp et al., 2020). By strengthening the immune system and reducing inflammation in the middle ear, *E. purpurea* may help prevent the progression of URIs to otitis media and mitigate its symptoms (Ogal et al., 2021). This can lead to fewer instances of ear pain, discharge, and hearing impairment, improving the overall quality of life for pediatric patients and their families (Wahl et al., 2008). Therefore, *E. purpurea* holds promise as a natural remedy for reducing the severity and duration of symptoms associated with

pediatric URIs and otitis media. Further research is needed to elucidate the optimal dosage, duration of treatment, and potential interactions with conventional therapies. However, its immunomodulatory and anti-inflammatory properties make it a promising candidate for integrative approaches to pediatric healthcare, offering potential benefits in symptom management and disease prevention.

Table 2. Overview of clinical trials evaluating effectiveness of *E. purpurea* in pediatric URI management

Age of participants	Treatment outcome	Adverse events	References
2-11 years	No significant difference in symptom severity or duration	Not specifically mentioned	(Taylor et al., 2003)
2-11 years	No significant difference in symptom severity or duration	Not specifically mentioned	(Barrett, 2004)
1-5 years	Reduced number of illness episodes, fever days, and treatment time	Rare, mild, and transient	(Cohen et al., 2004)
4-11 years	Symptoms improved on days 2-3; reduction in leukocyte count on day 8	One patient developed an allergic skin reaction	(Spasov et al., 2004)
2-11 years	Associated with a 28% decreased risk of subsequent URI	None reported	(Weber et al., 2005)

Table 3. Efficacy and safety of *E. purpurea* in pediatric otitis media treatment

Age range	Treatment outcome	Adverse events	References
1-10 years	No significant difference in treatment duration; reduced rate of biological characters usage in the *Echinacea* group	None reported	(Wustrow, 2004)
1-5 years	*E. purpurea* was associated with a borderline increased risk of having at least one episode of OM during the 6 months	Not specifically mentioned	(Wahl et al., 2008)

5. Clinical evidence on the efficacy of *E. purpurea* in children

The clinical efficacy of *E. purpurea* in treating pediatric URIs and OM has been explored in numerous studies with varying outcomes (Tables 2 & 3). Research indicates that *E. purpurea* may reduce the duration and severity of symptoms in some pediatric populations, though results are not universally conclusive. Studies often compare the effects of *E. purpurea* against placebos or standard care, focusing on outcomes like symptom relief, duration of illness, and incidence of secondary infections. While some trials report modest benefits, emphasizing shorter illness durations and reduced symptom severity (Cohen et al., 2004; Spasov et al., 2004; Weber et al., 2005), others find no significant difference between *Echinacea* treatment and control groups (Barrett, 2004; Taylor et al., 2003). Variability in study design, *Echinacea* preparations, dosages, and participant characteristics contribute to these mixed results. Despite these discrepancies, *E. purpurea* is generally well-tolerated with a safety profile comparable to placebo in most pediatric studies. The evidence suggests potential value in *E. purpurea* as an adjunctive treatment for URIs, warranting further research to define optimal use parameters. For example, Ogal et al. (2021) found that long-term use of *E. purpurea* significantly reduced the incidence and duration of URIs and their complications, including OM, in children aged 4-12 years, and also led to a substantial decrease in antibiotic prescriptions, highlighting its effectiveness in preventing URIs and reducing the need for antibiotics in pediatric patients.

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Research by Taylor et al. (2003) showed that *E. purpurea* is not effective in treating URI symptoms, and using the preparation increases the risk of rash in patients from 2 to 11 years old. A previous large-scale study (524 children) investigated the effectiveness of *E. purpurea* in improving treatment time, reducing the number of attacks, and increasing the safety of the product in treating URI (Weber et al., 2005). The results showed that *E. purpurea* has a positive effect in reducing the occurrence of subsequent URI in children. Recently, another study recommended the use of *E. purpurea* for long-term prevention of URI, helping to reduce URI complications and antibiotic use in children (Ogal et al., 2021).

Generally, the herb is considered safe for short-term use in children, with most studies reporting minimal side effects that are comparable to those observed with placebo treatments (Ogal et al., 2021; Weishaupt et al., 2020). Commonly noted adverse effects include rash, gastrointestinal discomfort, and allergic reactions, though these are typically mild and transient (Tables 2 & 3). Despite its good safety profile, there remains a need for caution, particularly in children with autoimmune conditions or those taking immunosuppressive medication, due to theoretical concerns about immune system stimulation. Rigorous long-term safety studies are lacking, suggesting the importance of further research to ensure the safe use of *E. purpurea* in pediatric care.

6. Safety profile and controversies

E. purpurea is generally regarded as safe for short-term use in adults and children when administered within recommended dosages (Wahl et al., 2008; Wustrow, 2004). Reported adverse effects are typically mild and transient, including gastrointestinal upset, allergic reactions, and rare cases of hepatotoxicity (Table 3). However, controversies surround the efficacy and safety of *E. purpurea* due to variability in product quality, lack of standardization among preparations, and conflicting findings from clinical trials (Weishaupt et al., 2020). Regulatory agencies such as the U.S. Food and Drug Administration (FDA) have issued warnings regarding unsubstantiated health claims and potential risks associated with *Echinacea* products, emphasizing the importance of evidence-based use and quality control measures. It is also important to note the theoretical concerns about immune system stimulation, particularly in children with autoimmune conditions or those taking immunosuppressive medication. Rigorous long-term safety studies are lacking, suggesting the importance of further research to ensure the safe use of E. purpurea in pediatric care.

7. Strategic approaches to *E. purpurea* use in pediatric respiratory conditions

Researching *E. purpurea* in pediatrics faces several challenges. Standardization is crucial due to variations in preparation methods affecting consistency and efficacy. Determining appropriate dosages for children is complex, requiring consideration of age, weight, and disease severity, with a need for age-appropriate formulations. Ethical and regulatory compliance is vital in pediatric research to ensure participants' safety and rights. Furthermore, potential interactions with conventional pediatric medications necessitate careful integration of *Echinacea* with standard treatments, highlighting the importance of monitoring for adverse effects and drug-herb interactions. These considerations are essential for advancing research and ensuring the safe use of *Echinacea* in pediatric populations.

Future clinical trials investigating *E. purpurea* for pediatric respiratory ailments should adhere to rigorous methodological standards. These include the use of randomized, double-blind study designs, the recruitment of adequate sample sizes, and the implementation of standardized treatment protocols to ensure the reliability and consistency of the results. Research should also examine its integration with conventional treatments, identifying synergistic benefits and optimal treatment strategies while assessing novel formulations for improved delivery and adherence. Importantly, longitudinal studies are necessary to ascertain the long-term safety and efficacy of *E. purpurea*, focusing on the potential for adverse effects and the importance of pharmacovigilance in monitoring its use in pediatric populations.

8. Study limitations

Primarily, the nature of a narrative review inherently involves selectivity in literature inclusion, which could introduce bias. Efforts were made to mitigate this through a structured approach to literature search and selection, yet the possibility of omitted studies relevant to the topic remains. This review emphasizes the need for a systematic review and meta-analysis to provide a more precise quantification of the effects of *E. purpurea* on pediatric upper respiratory tract infections and otitis media. Additionally, the search strategy was limited to specific databases, which may not have encompassed all relevant publications. Future studies could expand the range of databases searched to ensure a more exhaustive review of available literature. Lastly, the practical application of *E. purpurea* in treating pediatric URTIs and OM may require specifically designed products that cater to the unique physiological and metabolic needs of children. The current body of research lacks detailed exploration into optimal formulations and dosages suitable for pediatric use, pointing to a significant area for future investigation.

9. Conclusions

Pediatric URI and OM represent prevalent childhood illnesses that impose significant morbidity and healthcare burdens. *E. purpurea*, known for its immunomodulatory, anti-inflammatory, and antimicrobial properties, has garnered attention for its potential in managing these conditions. However, existing research on *E. purpurea* in pediatric respiratory infections presents mixed findings, suggesting the need for further investigation. Despite the inconclusive evidence, *E. purpurea* remains a popular herbal remedy for pediatric respiratory infections, highlighting the importance of evidence-based guidance for healthcare providers. In summary, while *E. purpurea* shows promise as a potential therapeutic agent for pediatric respiratory infections, further research is required to establish its role in clinical practice, ensure patient safety, and optimize respiratory health outcomes in children.

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Conflict of interest

The authors confirm that there are no known conflicts of interest.

Statement of ethics

In this study, no method requiring the permission of the “Ethics Committee” was used.

Availability of data and materials

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Supplementary File

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