MINI REVIEW

Can *Syzygium aromaticum* and *Eucalyptus globulus* Ease Respiratory Infection?

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Abstract

In response to the growing demand for effective treatments for respiratory infections, research has focused on the therapeutic properties of natural substances like *Syzygium aromaticum* (clove) and *Eucalyptus globulus* (Eucalyptus). Clove is rich in phytochemicals such as eugenol, which offers antimicrobial, anti-inflammatory, and antioxidant benefits in managing respiratory infections. Similarly, Eucalyptus contains eucalyptol, which is known for its antimicrobial and anti-inflammatory properties. This review systematically examines research on the active constituents of clove and Eucalyptus through a detailed analysis of scientific literature from databases such as Web of Science, Scopus, Google Scholar, and Research Gate. By assessing the phytochemical and pharmacological properties of these plants, the review highlights their therapeutic potential in treating respiratory infections. It also emphasises the need to explore further their use in developing innovative treatment strategies for respiratory health.

Keywords: *Eucalyptus globulus, pharmacological properties, phytochemical, respiratory infections, Syzygium aromaticum.*

Introduction

Respiratory infections (RIs) are infections that affect the respiratory system, including the nose, throat, airways, and lungs [1]. Clinically, RIs are classified into upper respiratory tract infections (URTIs), involving the nose, sinuses, pharynx, larynx, and trachea, and lower respiratory tract infections (LRTIs), which affect the airways and lungs below the larynx [2,3]. Common URTIs include the common cold, sinusitis, pharyngitis, laryngitis, and rhinitis, while LRTIs include pneumonia, bronchitis, and bronchiolitis [1–3]. These infections can be caused by viruses, bacteria, or fungi and they typically present with symptoms such as coughing, rhinorrhea, and nasal congestion [4,5].

Conventional methods to treat respiratory infections may involve using drugs that alleviate symptoms and eliminate the infection. Antibiotics are administered to cure bacterial infections when present, while other medications, such as bronchodilators, can aid in expectoration and relieve wheezing [4,6]. However, a drawback is that antibiotics have undesirable effects on bowel microflora and may lead to antibiotic resistance if used improperly [7,8]. At other times, respiratory illnesses are caused by viruses, so antibiotics will not be effective against them [5]. The prolonged use of antiviral drugs may also cause antiviral resistance [9]. The worldwide market for RIs treatment was valued at USD 33,534.13 million in 2021 [10]. According to research conducted by Business Research Insights, the RIs market is projected to escalate to a valuation of USD 53,207.21 million by 2027 [10]. This evidence underscores the necessity for interventions addressing RIs, encompassing traditional and complementary treatments.

In addition to conventional medicine, many individuals turn to herbal remedies for relief from respiratory infections [11,12]. Herbs have long been used in traditional medicine to treat respiratory conditions, which has prompted increased scientific interest in their therapeutic potential [12–14]. Plants such as *Syzygium aromaticum* (commonly known as clove) and *Eucalyptus globulus* (blue gum tree) contain various phytochemicals and metabolites that can help alleviate RIs [16].

S. aromaticum, commonly known as clove, refers to the aromatic flower buds widely utilized as a spice in Asian, African, Mediterranean, and Middle Eastern cuisines [14]. It also has been a staple in traditional medicine systems such as Ayurveda and Chinese medicine for centuries [13]. The essential oil derived from *S. aromaticum* buds is abundant in phytochemicals such as eugenol, α and β-caryophyllene, α-copaene, and methyl-salicylate, which serves a variety of medicinal purposes, such as promoting oral health, relieving pain, and exhibiting antibacterial and anti-inflammatory properties [13,15]. In respiratory infection, *S. aromaticum* can function as an expectorant and antimicrobial agent to alleviate the symptoms [16,17].

E. globulus, also known as the blue gum tree, is an evergreen tree in the Myrtaceae family [11,18]. Its essential oil is obtained from the leaves through steam distillation and has been extensively researched for its diverse properties and applications. Studies indicate that the oil possesses antimicrobial properties that are effective against bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA), serving as an expectorant to alleviate phlegm and relieve congestion [19,20]. Furthermore, eucalyptus oil, along with its constituent phytochemicals such as cineole, α-pinene, limonene, globulol, and flavonoids, has been shown to exhibit anti-inflammatory properties [11,21,22]. These components contribute to mitigating inflammation within the respiratory tract [20,22]. Additionally, the oil exhibits antiviral and antifungal properties, making it beneficial in addressing a variety of respiratory infections [6,22].

Studies on these plants concerning respiratory health remain limited over the years. Most studies have focused on phytochemical analysis, production and its application in several products [12,13]. A document that collates the most important and relevant studies, highlighting the main trends and developments concerning these

plants' potential for respiratory health, is necessary. Therefore, this mini-review delves into the potential impact of *S. aromaticum* and *E. globulus* in improving RIs by analysing each of the plants most popular phytochemicals. Additionally, it scrutinizes the pharmacological attributes of these phytochemicals and their roles in ameliorating RIs.

Methodology

This review examines the effects of *S. aromaticum* and *E. globulus* on improving RIs. It gathers information through a selection process, including research articles and narrative reviews that explore the plants' phytochemicals (natural chemicals) and pharmacological properties (drug-like effects). The inclusion criteria of this review consider studies conducted in both laboratory settings (*in vitro*) and on living organisms (*in vivo*) and focus on each plant's prominent phytochemicals and important pharmacological properties. Apart from that, non-English and retracted articles were excluded. Articles were systematically searched from various databases, including Web of Science, Scopus, Google Scholar, and Research Gate, to ensure a comprehensive analysis.

Results and discussions

Phytochemicals of *Syzygium aromaticum* and *Eucalyptus globulus*

S. aromaticum contains various phenolic compounds, including hydroxyphenyl propene, hydroxycinnamic acids, flavonoids, hydroxybenzoic acids, and eugenol, that improve RIs [15]. These compounds constitute the most prevalent bioactive components in the fresh plant and its essential oil, with a total phenolic content of around 9.07 gallic acid equivalent (GAE) mg/g [23]. Table 1 presents the major compositions and properties of clove.

Amongst the previously mentioned components of *S. aromaticum*, eugenol, α- and β-caryophyllene, and eugenol acetate are the primary and most prevalent phenolic compounds in fresh plant and essential oil [15, 24]. Eugenol has several pharmacological properties, including antioxidant capacity, antibacterial activity, neuroprotective ability, hypolipidemic efficiency, anti-inflammatory action, anti-carcinogenic effects, anti-diabetic effectiveness and therapeutic potential against respiratory distress [25]. Caryophyllene is soluble in ethanol but not in water. It has demonstrated local anaesthetic effects and antibacterial, anxiolytic, antioxidant, anti-inflammatory, and anticancer activities, including effectiveness against breast, cervical, prostate, and pancreatic cancers [15, 26]. Eugenyl acetate, a eugenol derivative, also showed antibacterial, anticancer, antioxidant, and antiviral properties [15].

Apart from that, compounds like chlorogenic acid, caffeic acid, gallic acid and p-coumaric acid from the phenolic acid group; kaempferol, myricetin, rhamnetin, quercetin and epicatechin from the flavonoids group; cyanidin compound from anthocyanin group, tannin also can be found in *S. aromaticum* as shown in Table 1.

E. globulus contains abundant phytochemicals, such as monoterpenes, oxygenated monoterpenes, sesquiterpenes, and triterpenic acids, which may help improve RIs (Table 1) [27–28]. These phytochemicals are commonly isolated from the leaves and have demonstrated broad-spectrum antiviral, antibacterial, anti-inflammatory, and antioxidant properties [11,19,22,29]. Prominent phytochemicals in *E. globulus* that aid in improving RIs are eucalyptol, α-pinene, limonene, globulol, and p-cymene [27]. Eucalyptol, also known as 1,8-Cineole, is a key component in *E. globulus* that helps to reduce RIs. This natural monoterpene (bicyclic ether) compound makes up 60-80% of *E. globulus* composition and primarily derives from the plant's leaves [22,30]. Eucalyptol is known for its antimicrobial, mucolytic and spasmolytic effects on the respiratory tract and is effective in treating respiratory infections [11,19]. It also demonstrates anti-inflammatory and antioxidant

properties, enhancing its therapeutic benefits in managing RIs [31,32].

The second most prevalent phytochemical found in *E. globulus* is α-pinene, typically comprising 7-11% of the total compounds in the plant [27,28]. A-pinene is a bicyclic monoterpene with a structure consisting of a six-membered ring fused to a four-membered ring and a double bond within the six-membered ring [20,32]. α-pinene has demonstrated therapeutic properties against upper respiratory tract infections due to its antimicrobial properties [11]. This compound also possesses anti-inflammatory properties that can soothe RIs [31].

Limonene is another intriguing component found in *E. globulus*, although it is present in smaller amounts (around 7%) compared to eucalyptol and α-pinene [27,28]. Limonene is a monocyclic monoterpene with a structure similar to α-pinene. The only difference is the number of cyclic structures; α-pinene has two bicyclic structures [20,32]. Limonene plays a crucial role in the plant's defense mechanisms and contributes to the biological activities of *E. globulus* [17]. However, research has indicated that limonene possesses anti-inflammatory and antioxidant properties, contributing to its therapeutic effects in respiratory infections [11,21].

p-Cymene, known as 1-isopropyl-4-methylbenzene, is another monoterpene compound that can be extracted from *E. globulus* leaves. p-Cymene typically comprises about 7% of the total *E. globulus* composition and shows promise as a therapeutic agent for managing respiratory infections due to its anti-inflammatory, antioxidant, antimicrobial, and analgesic properties [20,27,32]. Globulol is a bicyclic sesquiterpene alcohol that has been extracted from *E. globulus*. Around 6% of globulol can be found in *E. globulus* compositions [28]. Although globulol is a minor component in *E. globulus*, it has demonstrated strong antioxidant and antimicrobial properties, which could aid in reducing respiratory infections [28,31]. Other compounds that may help reduce RIs are β-pinene, β-myrcene and γ-terpinene (Table 1).

Pharmacological properties of *Syzygium aromaticum* and *Eucalyptus globulus*

Traditional medicine has used *S. aromaticum* as a respiratory, commonly used to address respiratory ailments such as coughs, colds, asthma, bronchitis, and sinusitis [33,34]. One method involves inhaling the aroma of hot clove tea during an aromatherapy session. In Asian cultures, it is customary to chew cloves to alleviate throat soreness and pharynx inflammation [33,34]. Additionally, chewing cloves after they have been heated is known to provide relief from intense coughing. *S. aromaticum* oil is also recognised for its expectorant, antiviral and antimicrobial properties, making it effective in treating respiratory disorders like colds, bronchitis, coughs, asthma, and other upper respiratory conditions [15,35]. On top of that, the active compound eugenol in *S. aromaticum* oil has been shown to disrupt the cellular membranes of bacteria like *Salmonella* and *Helicobacter pylori* [36,37].

Despite the many properties of *S. aromaticum*, studies on the plant's respiratory health are limited. A recent study by Chniguir et al. investigated the antioxidant potential of the plant aqueous extract and its protective effects on lipopolysaccharide (LPS)-induced lung in mice [38]. The study found that the plant inhibited the activity of myeloperoxidase, an enzyme in human neutrophils that can contribute to inflammation and oxidative stress. Specifically, the researchers showed that *S. aromaticum* could inhibit the generation of reactive oxygen species, superoxide anion, and hydrogen peroxide by human neutrophils. Furthermore, the study demonstrated that *S. aromaticum* had anti-inflammatory effects in a mouse model of LPS-induced lung inflammation. When *S. aromaticum* was administered intraperitoneally to mice before LPS exposure, it reduced the influx of inflammatory cells and the total protein content in the bronchoalveolar lavage fluid, indicating a protective effect against LPS-induced lung inflammation. Based on the study, the antioxidant

and anti-inflammatory properties of *S. aromaticum* make it a promising candidate for developing new therapeutic approaches to treat lung inflammation and related respiratory disorders [38].

The traditional medicinal application of *S. aromaticum* for respiratory illnesses documented antiviral effects against various viruses, and their anti-inflammatory and antioxidant properties collectively underscore the potential significance of *S. aromaticum* and its phytochemical components in respiratory problems.

Various studies have been conducted to evaluate *E. globulus* efficiency in improving RIs. One study examined eucalyptol, a major component of *E. globulus*, to investigate its effects on respiratory tract immunity and overall immune function in rat models [20]. This study aimed to investigate the impact of eucalyptol on the respiratory and immune function of CD8 and CD4 cells, as well as alveolar macrophages. The findings indicated that low and moderate doses (30 and 100 mg/kg) of eucalyptol positively affected CD8+ T cells, enhancing respiratory immune function [20]. However, high doses (300 mg/kg) had an inhibitory effect and impaired overall immune function [20]. These results demonstrate that eucalyptol can strengthen the immune system in the respiratory tract, potentially reducing the risk of respiratory infections. However, it is important to note that dosage plays a crucial role, as high doses can have detrimental effects on the respiratory tract.

Several studies have been conducted to confirm the strong antimicrobial properties of *E. globulus*. Salari et al. investigated the impact of *E. globulus* on pathogenic bacteria isolated from patients with respiratory tract infections [29]. Their findings showed that *E. globulus* was able to kill the common respiratory pathogens, including *Staphylococcus aureus*, *Streptococcus pyogenes*, *Streptococcus pneumoniae*, and *Haemophilus influenzae* at concentrations of 512, 128, 64, and 64 mg/L, respectively [29]. Another study explored the antiviral properties of both *E. globulus* oil and its primary active compound, eucalyptol [39]. The results have demonstrated *in vitro* antiviral activity against the respiratory virus influenza A (H1N1) [39]. It was found that the *E. globulus* involves the inactivation of free virus particles and disruption of the viral envelope structure.

A study of late rhinosinusitis using a human *ex vivo* model mimicking the human nose found that eucalyptol effectively reduced mucus hypersecretion [30]. The research involved treating nasal slice cultures with lipopolysaccharides to simulate bacterial infection in late rhinosinusitis, significantly increasing mucin-filled goblet cells. However, the group treated with eucalyptol showed a significant reduction in the number of mucin-filled goblet cells compared to the lipopolysaccharide-treated group [30]. At a molecular level, eucalyptol significantly decreased the expression levels of the mucin genes MUC2 and MUC19, associated with reduced NF-κB activity [30].

In a research study that investigated the impact of eucalyptus inhalation on upper respiratory tract infection (URTI) in 208 children aged 5-15 years [40], the participants were treated by inhaling 2 drops of eucalyptus oil mixed in 750 mL of hot water every 3 hours for 15 minutes over 3 days. The control group only received water vapour. The study revealed that eucalyptus fumigation notably relieved symptoms associated with various upper respiratory infections (URIs), such as colds, rhinitis, sinusitis, pharyngitis, otitis, and laryngotracheitis compared to the control group [40]. Table 2 shows more *in-vitro*, *in-vivo* and clinical trial studies involving *S. aromaticum* and *E. globulus* in treating RIs.

Limitations and future directions

Several limitations and gaps must be addressed despite *S. aromaticum* and *E. globulus* showing promising results in improving RIs. The current studies showed that varying protocols and methodologies for scientific research and clinical studies, such as actions in dosage variation, formulations, and delivery systems, create

challenges in drawing consistent conclusions about their efficacy. Additionally, some studies may point to potential drug interactions when these two plants were administered to the patients, there is also a need for more research addressing these plants' interactions with drugs, toxicity and side effects, particularly in diverse populations.

To overcome these limitations, future studies should prioritise conducting standardised clinical trials, mainly focusing on the formulations, dosage, and delivery systems, to assess the effectiveness and safety of *S. aromaticum* and *E. globulus* in treating respiratory infections. Additionally, it would be beneficial to explore the underlying mechanisms of action of the active compounds in these plants, especially their molecular mechanisms. Drug interaction studies can also be intensified to identify any adverse effects or contraindications of these plants with the commercialised drugs in the market. More toxicity assessments, including *in-vitro* and *in-vivo,* can be done to understand these plants' safety profiles better, focusing on long-term use and effects in vulnerable populations.

Conclusion

This mini-review highlights the potential benefits of *S. aromaticum* and *E. globulus* in improving respiratory infections (RIs). Key findings indicate that *S. aromaticum* contains bioactive compounds such as eugenol, caryophyllene, and eugenol acetate, which have antimicrobial, anti-inflammatory, and antioxidant properties. *Similarly, E. globulus* is rich in eucalyptol, α-pinene, and limonene, known for their antibacterial, antiviral, anti-inflammatory, and antioxidant effects. These compounds suggest a multifaceted approach to alleviating RIs, supported by both *in-vitro and in-vivo* pharmacological studies. The significance of these insights lies in their potential to enhance current RI treatments. Integrating *S. aromaticum* and *E. globulus* into conventional treatment presents an opportunity to develop more effective management strategies that address the limitations of existing treatments. This integration could be particularly valuable in light of rising antibiotic resistance, providing alternative options that may improve patient outcomes. However, the limitations and gaps should be addressed, especially regarding toxicity issues and unstandardised clinical trials. These plants can potentially become alternative treatments for RIs, and it is essential to understand their safety and effectiveness thoroughly. The findings of this review underscore the need for healthcare practitioners to consider integrating these plants into treatment protocols for RIs. By fostering collaboration between traditional herbal medicine and modern medical practices, the therapeutic options can be enhanced, promoting better health outcomes for patients suffering from respiratory infections.

Conflict of interest:

The authors have no conflict of interest to declare.

Authors' contribution:

P. M. R.: Writing - Review & Editing, Project administration; M. N.M.B.: Review & Project planning; N.H.C.B.: Review & Project planning; M. A. A. M.: Software, Formal analysis, Methodology, Writing - Original Draft; M. F. Z: Formal analysis, Writing - Review & Editing; W. I. W. I.: Writing - Review & Editing;

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Table 1. Bioactive compound and applications of *Syzygium aromaticum* and *Eucalyptus globulis*.

Plant	Compound	Proportion (%)	Applications	Sources
Syzygium aromaticum	Eugenol	74.28	Antimicrobial, insecticidal, anti-inflammatory, wound healing, antioxidant, anticancer (breast, prostate, colon, gastric, and skin cancer)	[25]
	Caryophyllene (α and β)	24.80	Anti-carcinogenic, anti-inflammatory, anxiolytic, antioxidant, anaesthetics effects, potential use as a chemosensitizer	[26]
	Eugenol acetate	2.70	Antimicrobial, anti-inflammatory, antibacterial, use in perfumes because of volatile nature	[25]
	α-copaene	0.17	Antimicrobial, antiproliferative, antigenotoxic, antioxidant, cytotoxic activity	[41,42]
	Methyl salicylate	0.20	Flavouring agent, antibacterial, anti-irritant, antiproliferative	[14, 15]

Eucalyptus globulis	Eucalyptol	60-80	Antibacterial, antifungal, antiviral, anti-inflammatory, cough suppressant, antioxidant and decongestions	[22]
	α -pinene	7-11	Anti-inflammatory, antimicrobial, bronchodilator, cough suppressant	[23]
	Limonene	7	Anti-inflammatory, antioxidant	[25]
	p-cymene	7	Antioxidant, anti-inflammatory, antiviral, antibacterial, antifungal,	[23]
	Globulol	6	Antimicrobial, antioxidant	[23]
	β-pinene	3	Analgesic (pain-relieving), anti-inflammatory, antibacterial, antioxidant	[25]
	β-myrcene	1-7	Analgesic, anti-inflammatory, antibacterial, antioxidant	[22]
	γ-terpinene	1-3	Antioxidant	[24]

Table 2. Studies related to using *S. aromaticum* and *E. globulus* for treating respiratory infections.

Compound	Extract type	Treatment	Results	Ref
S. aromaticum	Clove aqueous extract	Clove extract on the respiratory syncytial virus (RSV) infected HEp-2 cells.	Clove extract exhibited potent anti-RSV activity, appearing virucidal as it directly targeted RSV particles during the early stages of viral infections.	[43]
	Clove mouthwash	Clove mouthwash for the intervention group and chlorhexidine for the control group (twice daily for 5 days) to reduce ventilator-associated pneumonia (VAP) for ICU patients.	The intervention group (clove mouthwash) experienced a reduction in VAP infection compared to the control group. The risk of VAP was 2.06 times higher in the control group than in the clove mouthwash group.	[44]
	Clove essential oil	Clove essential oil on respiratory tract pathogens such as *Streptococcus pneumoniae, S. mutans, S. pyogenes, Haemophilus influenzae, H. parainfluenzae,* and *Moraxella catarrhalis.*	Clove oil exhibited antibacterial effects against all tested bacteria, with the strongest inhibition observed on *S. pyogenes*.	[45]
		Clove essential oil treatment on respiratory infection-related bacteria: *Streptococcus pyogenes, S. agalactiae, S. pneumoniae, Klebsiella pneumoniae, Haemophilus*	All respiratory infection-related bacterial growths were inhibited when treated with clove essential oil. S. pneumoniae and S. maltophilia showed the highest inhibition.	[46]

		influenzae, *Staphylococcus aureus* and *Stenotrophomonas maltophilia*		
		Clove oil on the outer membrane protein of *Pseudomonas* spp	The outer membrane protein with molecular weights of 42.7 kDa and 79.4 kDa disappeared after treatment which contributes to the antibacterial properties of the clove oil.	[47]
Eucalyptus globulus	*Eucalyptus* essential oil	Albino Wistar rats acted as the anti-inflammatory, analgesic and antipyretic model (orally treated with the essential oil).	*Eucalyptus* essential oil showed anti-inflammatory, analgesic and antipyretic effects on the rat models.	[22]
	1,8-Cineole enteric-coated capsules (Soledum®)	Every patient received 90 mg Ingavirin® (antiviral) capsule once daily. In addition, the treatment group also 200 mg received Soledum® capsules (3 capsules a day) for 4–9 days.	Patients treated with Ingavirin® and Soledum® exhibited a significant reduction in cough frequency and other symptoms of acute bronchitis compared to antiviral treatment alone.	[48]
	Isolated eucalyptol	Peripheral blood monocytes isolated from 12 healthy volunteers were used as a model to study inflammatory responses in asthma and chronic obstructive pulmonary diseases.	Eucalyptol reduces the release of inflammatory mediators (IL-1β, IL-6, IL-8, TNF-α) that cause an inflammatory reaction, suggesting that eucalyptol helps to suppress airway inflammation.	[49]
	Eucalyptol (Soledum®) capsule	Thirty-two patients were randomly assigned to receive	Soledum® treatment reduced steroid dependence in asthma	[50]

	either 200 mg of Soledum® or a placebo for 12 weeks, in addition to the typical steroid treatment for asthma patients.	patients. The capsule also acted as an anti-inflammatory and mucolytic agent in the tested patients.	
Eucalyptol gelatin capsule	152 acute rhinosinusitis patients were split into two groups: eucalyptol treatment and placebo.	Patients who received eucalyptol gelatin capsules showed an improvement of over 80% after seven days, compared to the placebo group which showed less than 50% improvement.	[51]

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