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A REVIEW ON EUCALYPTUS ESSENTIAL OIL IN THE TREATMENT OF CHRONIC ABSTRUCTIVE PULMONARY DISEASES

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ABSTRACT

1,8 cineol which is also known as eucalyptol is the main component of eucalyptus oil it is commonly known as Nilgiris which can be extracted from *Eucalyptus globules* which belongs to the family *Myrtaceae*. Eucalyptol is the organic compound having two isoprenes (2 methyl 1,3 butadiene). In this review we study about the effect of eucalyptol in the treatment of chronic obstructive pulmonary diseases (COPD). As for studies chronic obstructive pulmonary diseases is characterized by the persisting lung inflammation and air flow limitation which is caused due to the inflammatory mediator cytokinin, leukocytes. The mechanism involves in COPD is transforming growth factor which is the key of cytokinin induces the epithelial mesenchymal transition which leads to airwall remoulding (asthma, copd). Researches have been proven that 1,8 cineol decreases the mRna and protein level in epithelial mesenchymal transformation inducing air wall remoulding and there by treats and reduces the versioning of conditions of asthma and COPD.

KEYWORDS: *Eucalyptus oil*, 1,8 cineol, isoprene, essential oil, antispasmodic, ant mucolytic, anti-inflammatory and bronchodilator.

INTRODUCTION

Chronic obstructive pulmonary disease is characterized by the persistent lung inflammation and causes airflow limitation. 1,8 cineol which is also known as eucalyptol which is the extract of eucalyptus has shown with the benefits in the treatment of lung cancer and COPD. As per Alaa S. Tulba et al,[1] Eucalyptol oil (EPO) showed cytotoxic and anti-proliferative activities on the A549 cell viability which indicated the effectiveness of oil constituents

against lung cancer. NA YU et al,[2] describes that Eucalyptol is a natural organic compound of many plant essential oils, mainly extracted from Eucalyptus oil. This compound, a colourless liquid, is traditionally used to treat respiratory disorders due to its Secreto lytic and anti-inflammatory properties in the airways. Clinical trials have confirmed that 1,8-cineole improves ciliary beat frequency of the mucus membrane, and exhibits Secreto lytic and broncho spasmolytic properties. After COVID 19 pandemic, researchers have recognized COVID-19–linked severe co-infections such as mucormycosis, aspergillosis, coccidioidomycosis, and saccharomyces's.

Azole based drugs like fluconazole, itraconazole and ketoconazole are widely used as anti-fungal drugs due to chronic administration of antifungal drugs development of resistance[3] which can be managed with the administration of eucalyptol with antifungal drugs.

1,8-cineole is a saturated monoterpene present in various plant species such as *Eucalyptus, Rosmarinus, Psidium, Croton,* and Salvia but high concentrations of 1,8-cineole can be obtained from *Eucalyptus nicholii (> 80 %).* Clinical trials have confirmed that 1,8-cineole improves ciliary beat frequency of the mucus membrane, and exhibits secretolytic and broncho spasmolytic properties.[4]

Lisa Joy et al,[5] study states that 1,8-cineole interacted with relevant mediators of pathophysiological pathways of COPD and identified receivers and membrane channels, oxidative stress, transcription molecules and expression of cytokines, cell adhesion molecules and neutrophil chemotaxis, pro-inflammatory cells, proteases and remodelling as potential therapeutic targets. The authors concluded from these findings that eucalyptol (1,8-cineole) showed effective treatment option as the anti-inflammatory drugs in asthma and COPD.

Chronic Obstructive Pulmonary Disease (COPD) involves persistent airflow limitation due to chronic inflammation in response to noxious particles or gases, most commonly from cigarette smoke. Causes of COPD includes.

METHODOLOGY

Plant details

Eucalyptus oil is obtained by steam distillation and rectification from the fresh leaves or the fresh terminal branchlets of various species of Eucalyptus which belongs to family Myrtle (Myrtaceae). Eucalyptus is rich in 1,8-cineole.[6] Eucalyptus oil is a colourless or pale-yellow

liquid with an aromatic and camphoraceous odour and a pungent and camphoraceous taste. The plant contains 0.5-3.5% essential oil content with the main component of 1,8-cineole (about 70% or more) with some minor components like α-pinene (2-8%) and camphor (> 0.1%). The primary use of eucalyptus oil includes the treatment of cough, cold, bronchitis, and symptomatic activity.

Fig. 01: Eucalyptus leaves and tree.

Method of extraction

1. Distillation

1. **Steam Distillation**: This is the most widely used and preferred method for producing essential oils on a large scale.

- Process: Steam is passed through the selected part of plant with the increased concentration required essential component. The steam and oil mixture is then cooled, and the oil separates by the water and can be collected.

➢ Advantages: Produces pure eucalyptus essential oil with a high concentration of the desired components, like 1,8-cineole. Allows for large-scale production and is a standardized industry practice.

➢ Disadvantages: Requires specialized equipment and can be more expensive to set up than some other methods. High temperatures can potentially affect the oil's therapeutic properties if not managed properly.

2. **Hydro distillation**: A simpler and more traditional method where the plant material is directly boiled in water.

- Process: Eucalyptus leaves are submerged in water and heated, creating steam that carries the essential oil. The vaporized oil and water are then condensed and the oil is separated from the hydrosol.

- Advantages: Simple process, doesn't require complex equipment. Can be a viable method for small-scale extraction.
- Disadvantages: Can be a slower process compared to steam distillation. Oil components might be susceptible to hydrolysis and thermal decomposition at the higher temperatures involved. May not yield as high a concentration of oil as other methods.

3. **Water and Steam Distillation**: Combines aspects of both water and steam distillation, with plant material immersed in water and steam also introduced**.**

2. Solvent Extraction

- Process: Plant material is treated with a solvent (e.g., ethanol) to dissolve the essential oils and other compounds. The solvent is then separated, often through processes like distillation and rotary evaporation the required essential oil can be obtained.
- Advantages: Can extract a broader range of compounds, including those with higher molecular weights. Offers flexibility in solvent selection and can potentially be more efficient for extracting certain components.
- Disadvantages: Solvent residues can be a concern for some applications, especially in food and pharmaceuticals. This method can be laborious, duration-intensive, and may involve the use of hazardous solvents**.**

3. Supercritical Fluid Extraction (SFE)

- Process: Uses supercritical carbon dioxide (CO2) as a solvent. The CO2 penetrates the plant material, extracting the essential oil, and then the pressure is reduced, allowing the CO2 to return to a gaseous state, leaving the oil behind.
- Advantages: Considered a "green" extraction technology due to the use of a natural solvent and elimination of solvent residues in the final product. Can extract essential oils at lower temperatures, potentially preserving the delicate compounds.
- Disadvantages: Can be a more expensive method due to the specialized equipment and operational costs.

Conclusion: In the above methods distillation and solvent extraction methods are widely used in the extraction of eucalyptol (1,8 cineole)

Different marketed formulations of eucalyptol include

Pharmaceuticals

1) **Oral Medications**: these are the pharmaceutical products men for the administration of drugs through the oral route. Eucalyptol is found in cough syrups and throat lozenges for its potential respiratory benefits, such as helping to loosen mucus and clear airways. The eucalyptol is used in the formulation of enteric-coated capsules containing 1,8-cineole are used in treating inflammatory respiratory disorders like the common cold, bronchitis, sinusitis, bronchial asthma, and COPD.

- Inhalants: eucalyptol is used in the formulation of inhalers used in relieving nasal congestion and soothing irritated airways, particularly during colds and respiratory infections.
- Topical Rubs and Balms: Eucalyptol is used in topical rubs and balms for relieving minor aches and pains in muscles and joints, and for providing a soothing sensation for chest congestion.

2) **Oral care products**

- Mouthwashes: many of the formulations contain Eucalyptol in the formulation of mouthwash for its antibacterial properties and ability to freshen breath, combat dental plaque, and potentially help reduce gingivitis.
- Toothpastes: Eucalyptol is included in toothpastes for its antimicrobial effects and refreshing taste, helping to fight bacteria that can cause tooth decay and gum disease.

3) **Cosmetics and personal care products**

- Fragrances: Due to its pleasant spicy aroma and taste, Eucalyptol is used as a fragrance component in perfumes, body powders, and other cosmetic products.
- Skincare products: Eucalyptol is added to creams and lotions for its cooling and soothing effects on the skin, and its potential in treating and preventing acne due to its anti-inflammatory properties.

Due to the potential effect of eucalyptol, it is also used as

- Flavouring Agent: Eucalyptol is approved by the US FDA for use in foodstuffs to enhance odour and flavour, particularly in items like baked goods, confectionery, and beverages.
- Essential Oils and Blends: Eucalyptol is a prominent component in eucalyptus essential oil and can be found in various other essential oils like rosemary and sage. These oils are used in aromatherapy for their potential benefits in reducing pain, depression, and promoting relaxation and respiratory support.

- Cleaning Products: Eucalyptol's antimicrobial and antiseptic properties make it suitable for use in disinfectants and cleaning products.
- Insecticides and Repellents: Eucalyptol is used in products designed to repel insects

Fig. No. 02: Marketed formulations of eucalyptol.

Disease related

Chronic obstructive pulmonary disease (COPD) is a group of lung diseases that block airflow to and from the lungs, making it difficult to breathe. The two main types are chronic bronchitis and emphysema. Some of mediators involve in the cause of chronic obstructive pulmonary diseases are

1. Chronic Inflammation[2]

- **Trigger**: Long-term exposure to irritants like tobacco smoke, air pollution, or occupational dust.
- **Cells Involved**: Neutrophils, macrophages, CD8+ T lymphocytes.
- **Effect**: Inflammatory cells release proteases and cytokines, damaging lung tissue and stimulating mucus production.

2. Airway Remodelling and Narrowing

- **Goblet cell hyperplasia** → Increased mucus production.
- **Subepithelial fibrosis** → Thickening of the airway walls.
- **Smooth muscle hypertrophy** → Further airway narrowing.
- **Result**: Obstruction of airflow, especially during exhalation.

3. Emphysema (Alveolar Destruction)

- **Loss of alveolar walls** due to protease activity (e.g., elastase) exceeds antiprotease protection (e.g., α1-antitrypsin).
- **Loss of elastic recoil** → Air trapping.
- **Decreased surface area for gas exchange** → Impaired oxygenation and CO_2 elimination

4. Asthma

Asthma is a chronic respiratory condition that affects the airways of the lungs, causing inflammation and narrowing. Which causes the decreased airflow and failure of breathing.

Mechanism involved in the COPD

1. Cytokines

Small proteins that regulate immunity, inflammation, and haematopoiesis.

Pro-inflammatory Cytokines **(drive the inflammatory response)**

- Tumour Necrosis Factor-alpha (TNF-α)
- Interleukin-1 (IL-1α, IL-1β)
- Interleukin-6 (IL-6)
- Interleukin-17 (IL-17)

Anti-inflammatory Cytokines **(limit inflammation)**

- Interleukin-10 (IL-10)
- Transforming Growth Factor-beta (TGF-β)

2. Chemokines

Chemotactic cytokines that attract immune cells to the site of infection.

- IL-8 (CXCL8): -recruits' neutrophils
- MCP-1 (CCL2): -recruits' monocytes/macrophages
- RANTES (CCL5): - attracts T cells and eosinophils
- MIP-1α (CCL3): -attracts multiple leukocyte types

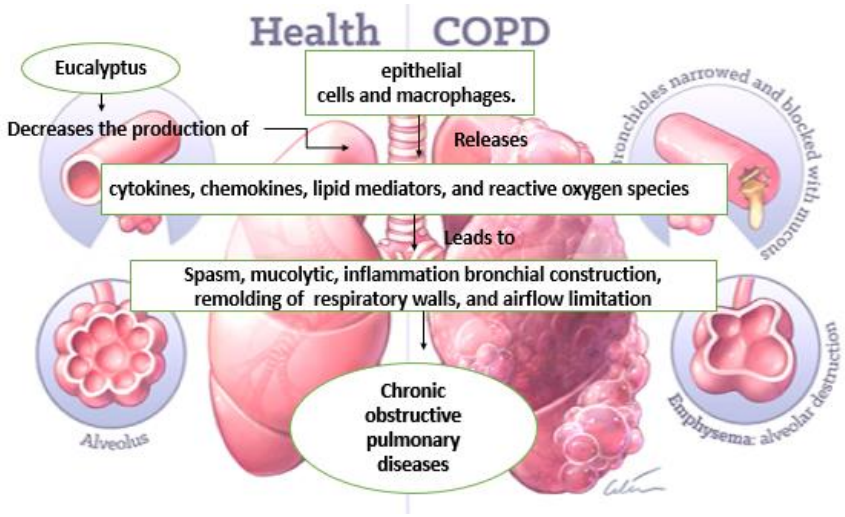

Fig. 03: Mechanism of eucalyptus on infected upper respiratory tract.

Other cell mediators that effect the lung include histamine, lymphocytes, and other inflammatory cell mediators which causes the chronic obstructive pulmonary diseases.

Eucalyptol can be obtained from various herbs as mentioned below.

Sl no	Plant	Species	Concentration
1	Eucalyptus	*Eucalyptus nicholii*	90% eucalyptol
2	Rosemary	*Rosmarinus officinalis*	14% - 64% eucalyptol
3	Bay leaf	*Laurus nobilis*	12.30%-24.60%
4	Tea tree oil		Less than 15%

Due to higher concentration of eucalyptol in the eucalyptus there by essential oil of eucalyptus is used in the treatment of chronic obstructive pulmonary diseases like emphysema, asthma, shortness of breathing, inflammation in lungs and remoulding of walls of lungs.

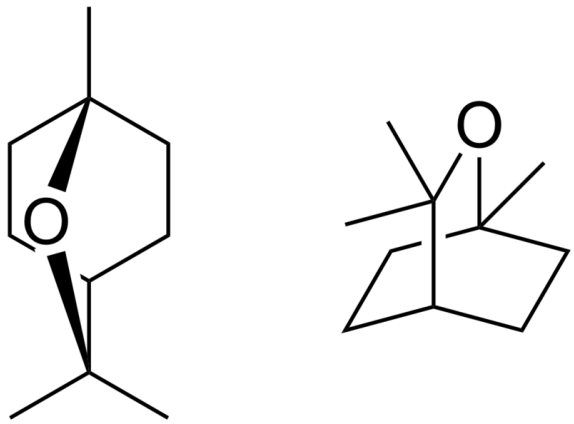

Fig. 04: 1,8 cineole (eucalyptol).

Method of extraction of eucalyptol for eucalyptus plant

1. Distillation

a. Water distillation

b. Steam distillation ‘

c. Water and steam distillation

2. Solvent extraction

3. Cold pressure extraction

4. Maceration

The method of formulation is simple for the extractions of essential oil for the extraction of eucalyptus essential oil the method of extraction includes extraction from fresh leaves of *Eucalyptus globules* by hydro-distillation method and stored in dark bottles at 4 °C for further studies.

Evaluation tests for nano emulsion and drug activity

Effect of drug in the treatment of COPD

1. Anti-inflammatory effect: - Inflammation is a natural response to injury or infection, characterized by redness, swelling and pain. The substance used to treat inflammation is anti-inflammatory agent.[2]

Mechanisms of Anti-Inflammatory Action

a) Inhibition of Pro-inflammatory Cytokines

- Eucalyptol suppresses the production of inflammatory mediators like TNF-α, IL-1β, IL-6, and PGE2, which play major roles in chronic inflammation.

b) Inhibition of NF-kB Pathway

- Eucalyptol downregulates NF-kB, a transcription factor involved in regulating immune response and inflammation.

c) COX-2 Inhibition

- Eucalyptus oil reduces cyclooxygenase-2 (COX-2) expression, an enzyme responsible for the formation of pro-inflammatory prostaglandins.

2. Antispasmodic: - The ability of a substance to prevent spasms, particularly those occurring in smooth muscle.

Mechanisms of Antispasmodic Action

a) Calcium Channel Modulation

Eucalyptus oil components may inhibit voltage-dependent calcium channels, reducing calcium influx into smooth muscle cells and thereby limiting contraction.

b) Reduction of Acetylcholine-induced Contractions

In vitro studies show eucalyptus oil can reduce acetylcholine-induced smooth muscle contractions, pointing to a cholinergic pathway inhibition.

c) Direct Smooth Muscle Relaxation

- Eucalyptol has a direct relaxing effect on smooth muscle, likely through modulation of intracellular signalling such as cyclic AMP (cAMP) or nitric oxide pathways.

3. Ant mucolytic: - It is the ability of substance to breakdown of mucus and thinning of mucus

Mechanisms of Mucolytic Action

a) Reduction of Mucus Viscosity

- 1,8-cineole alters the physical properties of mucus, reducing its thickness and stickiness, which facilitates easier clearance from the lungs and airways.

b) Modulation of Mucin Production

- It regulates mucin genes (like MUC5AC) that control mucus overproduction, especially in chronic respiratory conditions like asthma, COPD, and bronchitis.

c) Stimulation of Ciliary Activity

- Eucalyptus can enhance mucociliary clearance — the movement of mucus by tiny hair-like structures (cilia) in the airways — helping move phlegm out of the lungs more efficiently.

4. Antioxidant: - it is the imbalance between the oxidants (free radicals) and antioxidants which results in chronic inflammation and tissue damage the substance used to reduce the imbalance that is reduces the harmful reactive oxygen species is used as antioxidants.

- Eucalyptus is primarily does not shows the antioxidant property but it effectively reduces the harmful reactive oxygen species there by shows the antioxidative property of the compound.

- It also reduces the oxidative stress in the lungs

CONCLUSION

eucalyptus is anciently used in the treatment of chronic obstructive pulmonary diseases with the beneficial anti-inflammatory, antispasmodic, ant mucolytic and bronchodilator activities. During covid 19 also it is used in the treatment of chronic obstructive pulmonary disease conditions such as cold cough and other histaminic allergic reactions.

Literature review

1) Gyorgyi Horváth et, al. Essential oils in the treatment of respiratory tract diseases highlighting their role in bacterial infections and their anti-inflammatory action: describes that Based on WHO data, LRTIs and chronic obstructive pulmonary disease (COPD) have remained the top major killers during the past decade. EOs may possess a preventive role in the treatment of RTIs. The application of eucalyptus oil via inhalation seems to be the most effective way to cure patients, because of their volatile nature they can reach the site of action.
2) U. R. Juergens et, al. Anti-inflammatory Properties of the Monoterpene 1.8-cineole: Current Evidence for Co-medication in Inflammatory Airway Diseases 1,8-cineole is a saturated monoterpene present in various plant species (e. g. *Eucalyptus, Rosmarinus, Psidium, Croton,* and *Salvia*), with the main sources being eucalyptus leaves 1,8-cineole reaches the lungs and is exhaled via the peripheral airways thereby exposing its beneficial effects to the entire airways including the sinuses that are known as important source to promote infectinduced exacerbations.
3) Yanhong Wang et, al. Anti-Inflammatory Effects of 1,8-cineol (Eucalyptol) via NF-κB/COX-2 pathway in BEAS-2B cells andalleviates bronchoconstriction and airwayhyperreactivity in ovalbumin sensitized mice Asthma is a complicated chronic infl ammatory complications affecting airways in the lung, strongly associated with airway inflammation and airway remodeling, and characterized by airway hyperresponsiveness. 1,8-cineol decreases airway inflammation and macrophage activation in a mouse model of OVA-induced asthma. 1,8-cineol can inhibit TGF-β1-induced macrophage activation, including cell proliferation and migration. 1,8-cineol's inhibitory effects in an asthma model may be mediated by the NF-κB/p-P65 signaling pathway. Our findings indicate its potential use as a therapeutic medication against allergic asthma.

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6) R. Guo et, al. Herbal medicines for the treatment of COPD: a systematic review for effectiveness of herbal medicines for treating chronic obstructive disease. Considering the popularity of herbal medicine among chronic obstructive pulmonary disease patients, rigorously designed studies seems to be warranted.
7) Jie Liu1 et, al. Protective Effect of 1,8-Cineole (Eucalyptol) on Respiratory System: A Systematic Review and Meta-analysis from Animal Studies. This meta-analysis examines the anti-inflammatory and respiratory protective effects of 1,8-cineole in animal studies for the first time. We find that 1,8-cineole significantly inhibited inflammatory factors (TNF-α, IL-6, IL-1β, NF-κB) and inflammatory cells (neutrophils and macrophages), demonstrating a beneficial effect on the respiratory system.
8) Lisa Joy Juergens et, al. New Perspectives for Mucolytic, Anti-inflammatory and Adjunctive Therapy with 1,8-Cineole in COPD and Asthma: Review on the New Therapeutic Approach Independently of mono- or adjunctive therapy with 1,8-cineole, long-term therapy, because of its antiviral, antibacterial, antioxidant and anti-inflammatory activity, is to be recommended besides its effects to control systemic and peripheral lung inflammation, an area that is not generally reachable for standard inhalation therapies.
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prevalent among the COPD populations of the Nilgiris and requires immediate medical attention.

10) Anupam Maurya et, al. A concise review on Phytochemistry and Pharmacological properties of *Eucalyptus tereticornis* Smith. The leaf extract and oil have also been studied for their pharmacological activates like antihypergycemic, antibacterial antifungal, antioxidant larvicidal and myorelaxant property.

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