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Advancements in Respiratory Health: Evaluation of the Therapeutic Potential of 1,8-Cineole from Chronic Conditions to COVID-19 Era

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Abstract

After the pandemic wave hit the global population, the health community is concerned regarding the rising number of new inflammatory conditions associated with the COVID and other diseases.

This study delves deep into the therapeutic niche of 1,8 cineole, a bioactive compound found in cardamom extracts, with a focus on its potential to transform respiratory health. The article begins by closely looking on the relationship between stress induced by oxygen free radicals and inflammation in chronic airway diseases. This is especially seen in the idea of COVID-19 pandemic.

The article focuses on conditions such as COPD and asthma and their inflammatory cascades thus putting a light on the key role of 1-8-cineole in propagating inflammation. A connection between acute bronchitis and rhinosinusitis to major respiratory disorders is established here by fine examination of crossover between inflammatory pathways. A key aspect of this discussion revolves around the application of 1,8-cineole specifically in the form of RECOVEREEZ FORTE, as a potential treatment for COVID-19. This study not only shows quick recovery rates but also introduces a new confirmatory approach. This is by utilising saliva as an easily accessible and non-invasive specimen for follow-up of inflammatory markers.

The article relies on many randomised control trials for its evidence, thus showcasing 1,8-cineole's efficiency in reducing exacerbations. Thus, it improves the lung function and positively impacting the quality of life in conditions like rhinosinusitis, acute bronchitis, COPD, and asthma. It emerges as a game changer in the realm of respiratory care due to its ability to regulate inflammatory cytokines, suppress key enzymes.

In conclusion,1-8 cineole acts a bridging compound between traditional and modern approaches, addressing current health challenges. Though we know the limitations of the study, the article focuses on the compounds significant potential and pushes further study onto this area and potentially trying to modify the landscape of respiratory care.

Keywords: 1,8-cineole ,RECOVEREEZ FORTE , Chronic obstructive pulmonary disease, COVID ,Rhinosinusitis , corticosteroids

Introduction

The increasing prevalence of chronic airway diseases along with the global ageing poses a significant public health challenge for countries and the medical fraternity. The location along with its function and anatomy is such that it can be affected by various exogenous stress factors or reactive oxygen species (ROS)[1].In case of obstructive diseases like COPD and Asthma inflammation and oxidative stress plays a vital role in the pathogenesis. Oxidative stress can be described as an imbalance between the defensive ability of the body with its antioxidant activity versus production of reactive oxygen species.[2]

High levels of reactive oxygen species(ROS)is produced in individuals with asthma and COPD which is contributing to tissue damage and heightened oxidative stress[3,4]. The severity of both the diseases are influenced by both internal and external sources of ROS. The oxidative pathways and byproducts play a huge role in increasing the inflammation in asthma and COPD by affecting signal transduction pathways, activating redox sensitive transcription factors and modulating chromatin.This ultimately results in the expression of inflammation causing genes.[5,6]

Talking about obstructive diseases, other class of inflammatory diseases which could be the causative factors for these could be rhinosinusitis and acute bronchitis. Repeated episodes of these inflammatory conditions are

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associated with these major respiratory conditions. Along with this came the long and devastating Covid pandemic which added a spark and ignited all the existing inflammatory conditions especially the respiratory ones. In a population level and a financial point of level, this posed a huge threat foe the countries and we have to find a solution for this issue. This is one of the prime reasons to study the inflammatory aetiology and mechanisms of propagation for these inflammatory cascades. Novel methods could bring hope and give a healthier approach for the problems.

Crossover between inflammatory pathways of respiratory conditions

Sinusitis is a prevalent condition arising from viral or bacterial infections, with major share contributed by viral organisms. This is followed by buildup of unusually thick mucus and inflammatory mediators that hinder the mucociliary transports effectiveness. The excessive secretion pf mucus, coupled with edema and compromised mucociliary transport, obstructs drainage pathways, leading to symptoms like congestion, obstruction, pain and pressure.

The continuous mucous lining of the paranasal sinuses and nasal cavity often leads to concurrent inflammation. Clinically relevant definition of sinusitis involves mucosal inflammation accompanied by fluid stasis in the spaces. In acute cases, ostial obstructions primarily result from mucosal oedema, with potential exacerbations due to underlying anatomical abnormalities. It's crucial to differentiate between general mucous inflammation and sinusitis due to bacterial infection since the treatment approaches vary for each condition.[7]

While defining bronchitis, it is characterised by a persistent cough lasting more than 5 days, acute bronchitis sees approximately 50% of patients producing sputum which is purulent.This is an indication of shredden tracheobronchial epithelium and inflammatory cells[8].Usually quick diagnostic tests targeting specific pathogens are generally not recommended.The majority of acute bronchitis cases stem from virus causing infections, with key pathogens including viruses such as influenza virus A and B, parainfluenza virus, respiratory synctitial virus, the recent coronavirus, adenovirus and rhinovirus.If we properly study the literature, giving antibiotics is often not the first line treatment.[9]. Often, it emerges in tandem with a slight common cold, presenting a primary symptom of either a dry or productive cough. Despite its predominantly viral origins, over 50% of visits for acute bronchitis in medical practices lead to antibiotic prescriptions, on average.

COPD is one of the most studied and seen lung condition which is both chronic and irreversible.Both the self and acquired immunity is engaged here.It is most prominent in the bronchial walls of the small airways.It could be differentiated very well based on its presentation and pathology in the cases of emphysema and chronic bronchitis.Usually exacerbations are seen in COPD that are associated with increased inflammation in episodes. These exacerbations are triggered by various factors, including infections due to various pathogens like bacteria,virus,or even combined and associated with environmental factors.[10]

Finally, another inflammatory lung pathology entity, i.e Asthma. Usually it originates from a non pathogenic stimuli in the airways, asthma is marked by a chronic inflammatory reaction integral to its pathogenesis. This inflammation extends across all sections of the respiratory pathway.This also includes the upper respiratory tract and sinuses too.Independent of the type of asthma,the type of allergy or non immunological factors such as exercise,smoke or even age,the involved cells and cellular components in the inflammatory processes appear comparable.[11,12].

From the pathology of asthma, it is evident that rhinosinusitis can occasionally escalate into asthma attacks in susceptible individuals and also in the case of repeated attacks of acute bronchitis can be associated with chronic bronchitis which in turn is a itself COPD. Thus the importance of eliminating the inflammatory cascade in the early stages can on one hand settle the spread of inflammation and on other hand reduce the dependence on steroids and antibiotics. Resistance towards antibiotics is a major issue medical society and scientific community together is facing in this decade. Thus at any costs research and new drugs should be introduced to decrease the burden on the health community.

The unsettling rise of inflammatory diseases: Post COVID-19

On December 2019, Wuhan, China, there occurred a surge in pneumonia cases climbed really high that raised fear among the world but the cause remained unknown for a period[13]. By January 2020, it was confirmed to be a novel coronavirus(CoV) in a pneumonia patient by the Chinese Centre for central Disease control and prevention and it was later recognised as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).Distinct from previous coronavirus in a pneumonia patient, initially named 2019nCOV and later recognised as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Distinct from the previous coronaviruses

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like SARS-CoV and MERS-CoV, this marked the beginning of the pandemic, declared by the WHO in march 2020.[14]

Since then, covid has rapidly spread globally, infecting people in nearly every country. As of May 17, 2021, the confirmed COVID-19 cases surpassed 163 million, with over 3.3 million lives lost to the disease. After this COVID pandemic began, there occurred a huge rise of inflammatory conditions, especially in aged and ill people. The disease propagation involves an excessive immune response driven by cytokines, with multiple types of immune cells and inflammatory mediators playing crucial roles, as highlighted in various studies[15,16].This has triggered scientists across the globe to explore a range of anti-inflammatory and drugs to combat the intense inflammation associated with the condition. This review provides a comprehensive overview of how inflammation contributes to the pathogenesis of COVID-19, critically evaluates pharmacological agents addressing inflammation and the immunity in the context of COVID treatment and synthesises significant findings from the plethora of studies conducted thus far. The impact of COVID1-19 on global healthcare has significantly affected the economic burden. The search for effective therapeutic drugs to prevent, treat or mitigate COVID-19 manifestations remains a real need.

In this interesting study, initially the potential of cardamom extract was explored in reducing the inflammation by topical applications. This was pretty successful too. Later, along with the exceptional results in the niche of anti-inflammatory properties, the focus then shifted to investigating whether the bioactive compound within the cardamom extract i.e. 1,8-cineole could offer clinical benefit to COVID-19 patients. The exaggerated cytokine storm associated with immune response closely associated with propagation and severity, attracting for interventions capable of dampening the storm[17,18].

What is 1,8-cineol?

While looking in a compound level,1,8-cineol and other constituents like terpenes, including camphor and menthol, belong to the group isoprenoids(C5), composed of 2-isoprene subunits(C10). These compounds like sesquiterpenes(C-15) and steroid hormones(2*C15) and other substances such as glucocorticoids and tocopherols C20 are related to human isoprenoids. They have a different number of subunits, with tocopherols having more than sesquiterpenes share a connection with human isoprenoids like sesquiterpenes(C15.The initial indication of potential anti-inflammatory properties of 1,8 cineol came from its reported inhibition of cyclooxygenase pathway[19].Recognising that inflammatory mediators can induce airway hyper secretion by stimulating Cl secretion, recent findings indicate that the monoterpene 1,8-cineol exhibits a suppression similar to steroids, of arachidonic acid metabolism and in vitro cytokine production[20,21].

In the case of monocyte mediator production ,a dose dependent inhibition is demonstrated at therapeutic plasma levels, comparable in level to the effects of budesonide[22].Investigations under controlled set up reveals further observations revealing significant enhancements in lung function test[23].In non-controlled study, the administration of 200 mg of 1,8-cineole thrice daily, facilitated by enteric coated capsules, exhibited noteworthy inhibitory effects on leukotrieneB4(LTB4)and interleukin-1 beta-(IL-1b)in stimulated monocytes ex vivo[24].This helps in proving the growing branch of studies to find the potential of this magical drug.

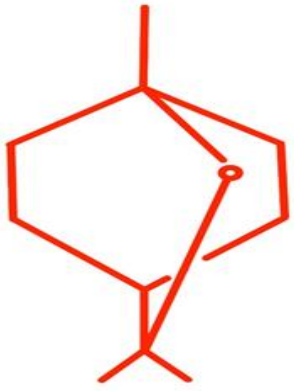

Fig.1- Structure of 1,8-cineole

Why and how is this compound a game changer ?

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1,8-cineole as discussed earlier emerges as a promising natural compound with multifaceted anti-inflammatory properties. Diving into its mechanisms of action reveals a comprehensive approach to mitigating inflammation. Firstly 1,8 cineole showcases its activity against inflammation by suppressing cytokines, including TNF-alpha and IL-6,1 that is key in the initiation and propagation of inflammation.

The compound intervenes in the inflammatory cascade by blocking the key enzymes such as cyclooxygenase-2 and LOX-5 that is responsible for the production of prostaglandins and leukotrienes, respectively. By slowing these mediators 1,8 cineole actively reduces inflammation, offering potential relief in conditions ranging from arthritis to respiratory disorders[25]

The balance of inflammation can be maintained by immune cells called macrophages,1,8 cineole seems to shift the balance towards the anti-inflammatory side and reducing the overall inflammation.

1,8 cineole also exhibit mucolytic properties in respiratory conditions. It helps to break down and thin mucus, that makes it easier to expel it out. This can be a particular advantage in conditions where excessive mucus production that causes airway obstruction[21]

In the Central Nervous System, cineole has shown great potential for reducing neuroinflammation. This could be attributes to its ant inflammatory and anti-oxidant properties, that finally acts as a neuroprotective action[2,26]

While the research and studies are still going on, results are found to be positive and more applications of this magical compound is there to revealed.

Evidence favouring the claims

On the context of respiratory diseases, the effect of 1,8-cineole has been studied extensively on various conditions and numerous patients. But here we discuss the extent of action of cineole on 4 main conditions, rhinosinusitis, acute bronchitis, COPD and Asthma. Double blind randomised, placebo controlled trial was conducted in all these cases.

Respiratory Condition	**Effects of 1,8-Cineole**
Rhinosinusitis	Significant reduction in symptoms, improved nasal cavity and sinus findings
Acute Bronchitis	Decreased bronchitis score, reduced coughing fits
COPD	Reduction in exacerbations, improved dyspnea, significant quality of life improvements
Asthma	Increased forced expiratory volume, improvements in the symptoms of asthma and quality of life

Rhinosinusitis

In a randomised study across the time period November 2000 to April 2001,152 patients were assigned. This demonstrated a significant reduction in symptoms sum score in the cineole group compared to the other placebo group after both 4th and 7th days of therapy P<0.0001)>.Merely 8% of cineole treated patients failed to exhibit an improvement exceeding 50% after 7 days, contrasting with 73% in the placebo group. Secondary outcomes, covering individual symptom scores favoured cineole group over placebo after both 4 and 7 days/Incidences of fever were negligible and comparable between groups. Rhinoscopic findings, particularly pertaining to the nasal cavity and sinuses, confirmed the clinical efficiency of cineole, revealing statistically significant differences. Subgroup analyses based on gender, allergy history, smoking status and baseline symptom scores did not alter the over arching positive outcomes in favour of cineole. Also, assessments by both physicians and patients

supported cineol's effectiveness. The adjunct use of a decongestant spray was very common among patients.B-scan ultrasonography was used to confirm the diagnosis of acute non purulent rhinosinusitis that revealed a clinically meaningful and statistically important difference revealing a clinically meaningful and statistically important difference favouring cineole after 7 days. C-reactive protein reductions were notably greater after verum treatment comparing to placebo with numerical evidence.Between the WBC counts and ESR rate of the two groups no obvious difference were found.While the control group saw no side effects,the cineole group noted mild to moderate adverse effects in 5 patients ., not related to medications. A good compliance was maintained across all patients during the 7 day treatment duration.[27]

Bronchitis

In a randomised control study that involved 242 patients with acute bronchitis from February 2010 to January 2011, both cineole and placebo groups exhibited comparable baseline characteristics wit mean ages at entry of 41.0 and 43.9 years and mean durations of acute bronchitis of 3.9 and 4.0 days respectively. Throughout the 10-day treatment period, medication almost remained unchanged and treatment compliance was consistently high in both groups. The primary outcome measures revealed a bronchitis score of covering various parameters showing a significant 14.6% decrease in the cineole group after 4 days, surpassing the 11.8% in the placebo group(p=0.0383**)**. This difference remained very distinct after 7 -10 days although statistical significance was not maintained. In secondary outcome measures, a statistical reduction in the number of cough episodes was observed in the cineole group after 4 days, (p=0.0001). However, when it was compared against a standard cough score, no characteristic difference between treatments were noted, emphasising the need for a precise definition in assessing symptom progress. Safety examinations revealed that adverse events within placebo group were generally unrelated to the study medication, except for one case of intolerance(heartburn). The difference in side effects between the two treatment groups was not both clinically relevant or significant in numbers. Reports of adverse events included gastrointestinal infection, otitis, sinusitis, eye burning, headache and stomach aches.[28]

COPD

The study involved 242 randomise COPD patients excluding 22 based on GOLD guidelines leaving 220 participants with well-matched baseline characteristics. Both the cineole and placebo groups with an average age of 62 years and a COPD duration of 13 years, exhibited balanced medication use. Throughout the treatment period, medication remained unchanged, barring exacerbations, ensuring consistent high compliance. In primary outcome, cineole demonstrated a decrease in the sum of exacerbations.The episodes where corticosteroids were given, statistically showed no significant differences between the groups. Secondary outcomes revealed no significant differences in lung function (FEV1 and FVC) after 6 months. However,the scores for dyspnoea in case of trouble in breathing, dyspnoea in the morning and dyspnoea at rest showed significant improvements in the cineole group. Also the Quality of life improvements, particularly In the SGRQ total symptom score, were statistically significant score for cineole compared to placebo (p0.0224)**.** A multiple criteria analysis, combining function of the lungs, dyspnoea and quality of life parameters, showed a statistically significant difference in favour of the cineole group(p=0.0024). Concomitant therapy of efficacy favouring the cineole group. Regarding side effects,22 patients were reported during treatment, with 17 unrelated to this study. While In the placebo group, 11 adverse events were unrelated and 2 were related (heartburn). The cineole group reported 9 adverse events with 6 unrelated. Three adverse events (nausea, diarrhoea, heartburn) were considered related to cineole, but the difference in adverse events between the groups was not clinically relevant nor statistically significant.[29]

In conclusion, cineole showcased efficiency in reducing exacerbations, improving dyspnoea and impacting certain quality of life aspects In COPD patients. Safety profiles and concomitant therapy were comparable, providing valuable insights into the potential benefits of cineole in COPD management.

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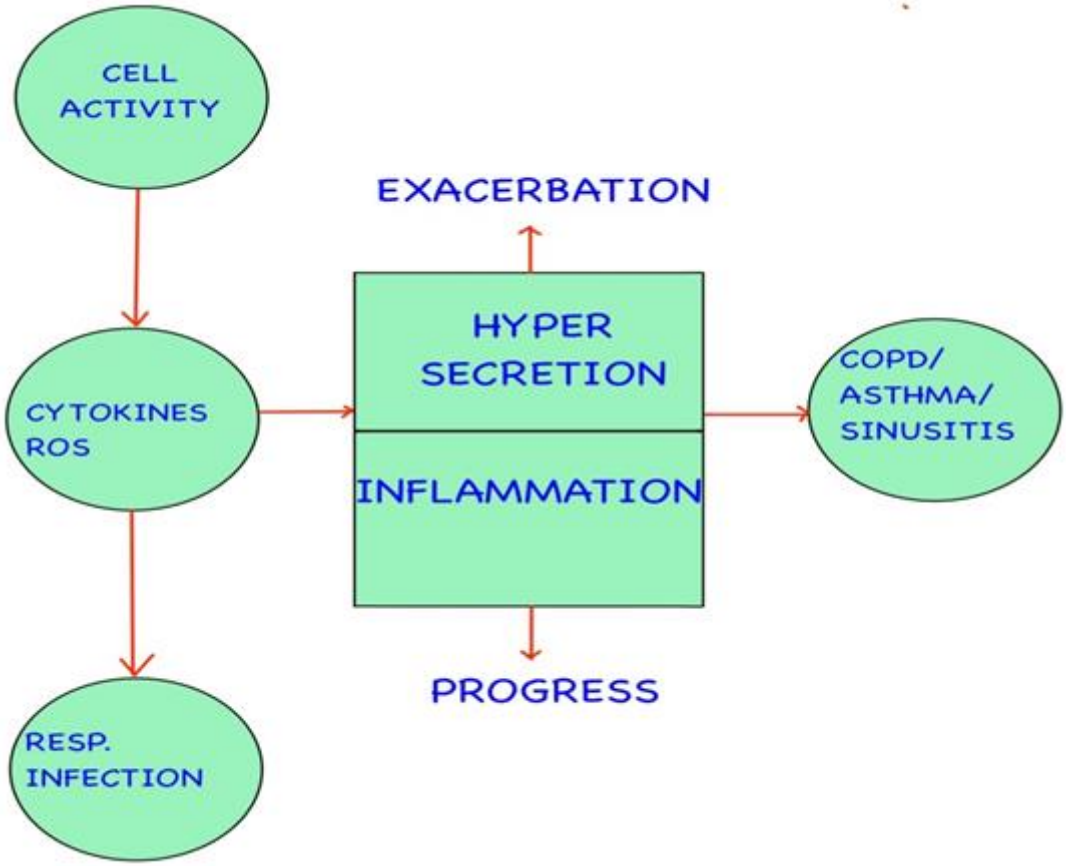

Fig.2 Pathophysiology of respiratory inflammatory conditions

ASTHMA

Between the period of November 2006 and January 2009, a large study of randomised controlled trial involving 247 real life asthma patients was conducted and the above patients received at least one dose of supervised medication . The 2 groups were arranged based on careful features that included age,asthma duration where the mean average age was 52.3 and 53.5 years respectively and a mean asthma duration of 14.7 and 15.3 years. In the full course of the study , baseline lung function were monitored and medications prescribed, included inhaled corticosteroids (ICS)along with long-acting beta agonists (LABA), anticholinergics and theophylline. Minimal medications were done, primarily occurring during exacerbations, while compliance remained consistently high across both groups, monitored through regular medication counts. The primary outcome measures, encompassing functions, asthma symptoms and improved quality of life, demonstrated good results after 6 months of treatment . The cineole group exhibited by a noteworthy mean increase of 0.31 litres in FEV1 compared to 0.20 litres in the placebo group. Moreover, significant better results were observed in nocturnal asthma scores and asthma quality of life questionnaire scores(AQLQ), with an overall statistical significance of p=0.0027.

Secondary outcome measures further supported the efficacy of cineole treatment. Significant increases in forced vital capacity (FVC) and PFR (peak flow rate) were noticed in the cineole group comparing to that of placebo group, with p-values of 0.0226 and 0.0197 respectively. Dyspnea scores, particularly at rest and during exercise also exhibited statistically significant differences between the two groups.[30]

Additional findings indicated significant Improvements in hyper secretion and cough frequency during the treatment period. Adverse events were minimal nor statistically important between the cineole and placebo groups during the 6 months.

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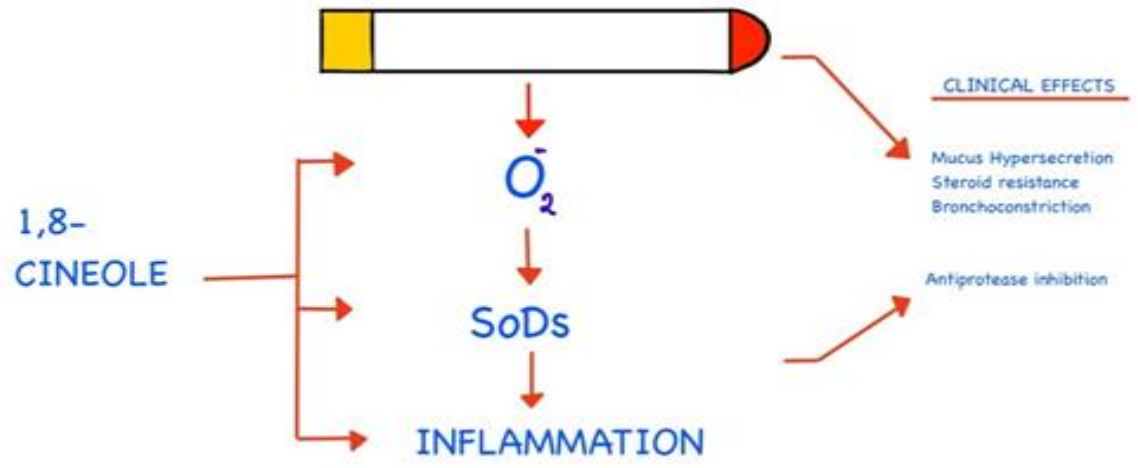

Fig 3.Smoking and environmental factors causing oxidative stress

Is cineole a substitute for steroids?

In a study involving thirty-three patients meeting entry criteria, the randomised administration of study medication was undertaken, with one patient eliminated due to existing illness. The protocol analysis on 32 patients revealed comparable lung function and glucocorticoid medication at baseline between the groups, except for a non-significant difference in the male-female ratio, resulting in a lower FEV1 in the placebo group.

Glucocorticoid dosages and asthma medications were evenly distributed and PFTs produced similar results. Throughout the 12-week study, all concomitant therapies remained unchanged upon exit. Notably, glucocorticoid saving effects were observed in individuals on 1-8 cineole group, with a mean reduction of oral glucocorticoids by 11.3%, compared to a significantly lower reduction of 2.4%in the placebo group(p=0.006). Cumulative reductions in prednisolone dosages favoured the cineole group, demonstrating a statistically considerable tolerance to dosage reductions at various visits.

Clinical effects of glucocorticoids were examined, revealing that prednisolone reduction had no significant impact on functions of lung and PEFR in the 1,8-cineole group. In contrast the placebo group showed a significant decrease in PEFR by 15.6% after the first reduction by prednisolone by 2.5 mg. Moreover,indication of salbutamol as a rescue medication rose in the placebo group after prednisolone reduction.

Scores for the frequency of dyspnoea were comparable at baseline but significant increased by 83.7% in the placebo group after prednisolone reduction indicating a greater impact on respiratory symptoms compared to the 1,8-cineole group. The safety profile of the drug was generally favourable with well tolerated adverse events and no serious adverse events reported. Adverse events were mostly mild, including URTI, back pain,headache,gastritis and heartburns, with no relevant abnormalities in routine blood tests.[31]

Studies suggest that 1,8-cineole a natural compound might help asthma patients by reducing the need of formal steroids while maintaining stability. While it shows promise, it’s not a direct alternative for steroids yet. Imagine a future where a fresh cardamom breath that is very refreshing in nature that reduces the reliance on current steroid asthma therapy, wouldn’t it be magical!

The Saliva Solution: A Novel Way Of Monitoring Inflammation In Covid-19

In view of the growing interest in saliva as a convenient and easy diagnostic specimen, a study was aimed to investigate the detection of three main inflammatory markers .Those were IL-6, TNF-ALPHA and IL10 which were then detected in the saliva of COVID patients using RT-PCR.IL-1, IL-6, TNF-alpha and even IL-10 are released by activated mast cells in the respiratory submucosa during major diseases. This earlyCOVID-19 research reveals the exacerbation of the inflammatory state and pathogenesis caused by these released cytokines[32].The main aim was to assess inflammation levels with a specimen that offers easy collection, which doesn’t require expert staff and also allow early detection and systematic monitoring. Also, the gene

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expression of inflammatory cytokines in patient saliva was checked and compared individually with whole blood to confirm the findings.[33–36]

Samples were collected from 135 patients, both blood and saliva (via standard venue puncture) under sterile conditions. Patients were asked to produce 2ml of saliva sample in a test tube. Both the samples underwent the extraction of the RNA genetic material and the later was then subjected to RT-PCR analysis. As discussed, earlier IL-10, IL-6 and TNF-alpha were monitored from both samples and quantified. The gene expression analysis of the inflammatory markers of IL-6, TNF-alpha and IL-10 in both samples were assessed in cycle threshold values.

Out of the total individuals,64 people (100%) expressed both TNF-alpha and IL-6-alpha genes, while only 7(5.19%) patients expressed IL-10 in saliva and blood specimens. The mean threshold values for IL-6 expression was 26.68+/-2.26 in blood and 28.53+/-3.11 in saliva. Similarly, for TNF alpha gene expression, the mean Ct values were 27.98+/-2.45 in blood and 28.92+/- in saliva. Finally, the observed Ct value for IL10 gene expression were 31.26+/- in blood and 30.11+/-4.12 In saliva. All these results can assure the these Inflammatory genes in patient saliva and blood specimen confirm the use of the saliva sample as a viable substitute alternative to blood.[37]

All the current cytokine markers investigations have predominantly relied on protein level assessment from plasma or serum ignoring the niche of gene level analysis. This study underscores the unique potential of utilizing non-invasive salivary technique for in depth insights. Saliva arises as unique specimen for various reasons such as easier, less stressful, and cost effective compared to the alternative collection specimens. The simplicity of saliva sampling allows a practical window in frequent monitoring, particularly in populations such as infants, children and the elderly. This becomes particularly difficult in situations where urine or blood sampling may prove impractical. Researchers globally recognise saliva as a valuable and accessible medium for diagnostic and prognostic purposes in various diseases.[38]

In spite of these numerous advantages, saliva has not yet gained the universal recognition as an analytical specimen. This lack of acknowledgement is due to the fact of insufficient data of its molecular composition and its relation with plasma levels. But in this study, we sought to address this gap by confirming the above inflammatory gene markers in blood and saliva of all the 64 COVID 1-19 patients. Thus, the comparable values across both the specimens especially concerning the expression of inflammatory genes confirms our findings to favour saliva over blood for monitoring and detecting these genes in COVID-19 patients.

Table.1Comparative Study on Saliva and Blood Samples in COVID-19 Patients

Inflammatory Marker	Saliva Ct Value	Blood Ct Value	Findings
IL-6	28.53+/-3.11	26.68+/-2.26	Comparable expression in both saliva and blood
TNF-alpha	28.92+/-	27.98+/-2.45	Similar expression in both saliva and blood
IL-10	30.11+/-4.12	31.26+/-	Limited expression, but comparable in both saliva and blood

1,8-cineole: a covid-19 treatment breakthrough?

After the pandemic aftermath surge, the world slowly started to develop vaccines and medications to fight the disease but no specific treatment was the gold standard in preventing the spread of inflammation across multiple systems. On that search for the golden drug there arose reports indicating the use of cardamom extracts in the inflammatory cytokine storm. These extract demonstrate the regulation of inflammatory cascade by suppressing

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reactive oxygen species (ROS)[26] , the weakening of inflammation by again suppressing NF-kB a pivotal regulator in the pathogenesis of inflammatory diseases[39], and the regulation nitric oxide(NO) synthesis[40].The therapeutic effects of cardamom extracts, particularly in respiratory ailments like asthma and COPD are attributed to predominant bioactive compounds such as alpha terpineol and 1,8 cineole[41]. The inhibitory effects of 1,8 cineole against pro inflammatory agents, including cyclooxygenase and lipoxygenase as indicated in reports, further support the anti-inflammatory properties of cardamom[25].In addition to its focus on anti-inflammatory effects and immune modulatory effects, there is increasing interest in medicinal interventions that could potentially disrupt the reaction between the viral spike protein and cellular angiotensin converting enzyme. This interaction facilitates the binding and entry of SARS-COV-2 into host cells[42,43].A drug called RECOVEREEZ FORTE was developed from standardised natural cardamom extract which had anti-inflammatory and anti-viral, immune modulatory properties[18].

In a randomised control trial involving 60 COVID patients,30 received the RECOVEREEZ FORTE TM (500 mg thrice a day) while the other 30 received standard care alone (control group). The average age was 39.67 years with 53.3% men. By the 5^{th} day,60% in the treatment group tested negative for COVID-19, compared to 23.37% in the control group. By the 10^{th} day,96.7% in the treatment group were negative, significantly more than the 43.3% in the control group(p-value<0.001)

A survival analysis showed a markedly increased survival time for the RECOVEREEZ FORTE TM group while looking on to the control group. The treatment group also demonstrated regulated expression of IL-6 in the plasma, indicating potential advantage over steroids, RECOVEREEZ FORTE TM also showed its efficiency in regulating CRP, LDH and D-DIMER levels in control. While observing the secondary outcomes, the total WBC counts were markedly lower in the treatment group on DAY 5,10 while the control group showed an elevated count. The lymphocyte counts in the treatment group remained still higher, pointing towards a milder disease state. No patients in the treatment group discontinued due to side effects.GI adverse events like gastritis, heartburn were observed in the treatment group.[44]

Finally, to summarise, the study points towards the fact that RECOVEREEZ FORTE TM may be a safe and efficient treatment for COVID-19 showing a faster recovery and a significant edge over oral steroids. While the study acknowledges some limitation such as a small sample group and a short follow-up period, indicating a careful interpretation. The results highlight the need for further research to asses long term benefits.

Table.2.Effects of RECOVEREEZ FORTE TM in COVID-19 Treatment

Outcome Measure	RECOVEREEZ FORTE TM Group	Control Group	Findings
COVID-19 Negative (Day 5)	96.7%	23.37%	Significant recovery in treatment group
COVID-19 Negative (Day 10)	Yes	43.3%	Controlled IL-6 expression in treatment group
IL-6 Regulation	Regulated	Elevated	Positive impact on inflammatory markers
CRP,LDH, D-DIMER Levels	WBC Counts (Day 5, 10)	Elevated (Control Group)	Favourable blood counts in treatment group

Conclusion

Our expedition into the therapeutic landscape of 1,8 cineole concludes with a compelling narrative that bridges realms of tradition and modernity. It also offers a glimpse into the future of respiratory care. A lot of issues such as steroid dependence, antibiotic resistance, cost cutting and prevention of chronic diseases could be addressed via this modality.

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As we look deep into this novel approach, there are limitation in this study as we have relatively small sample size and shorter span of monitoring done. More studies and follow ups have to be done so that this drug could be introduced into the current treatment plan. The evidences strongly suggest that the compound outperforms all the conventional treatment by a significant margin. This also covers the fact that is also helps is curtailing the current issues of drug resistance and propagation of mild diseases to life threatening complex conditions with less aggressive interventions.

Same can be said about the new investigatory approach. Cost effective and less invasive methods have to come onto the ground level so that the public are not reluctant for follow ups and disease transmission could be halted. And finally, by all these measures, easier and more accessible health care facilities would be provided to the public and the branch of research finds more of compounds and techniques to ease the burden.

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