Short Communication

Essential oils for COVID-19 management: A systematic review of randomized controlled trials

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Abstract

Essential oils can be a beneficial adjuvant therapy in managing coronavirus disease 2019 (COVID-19). This systematic review aims to evaluate the efficacy of essential oils in ameliorative COVID-19-related symptoms. Published studies reporting the efficacy of essential oils as adjuvant therapy for COVID-19 were screened on Scillit, Scopus, SciFinder, and PubMed (December 7th, 2022). Inclusion criteria include the randomized controlled trials (RCTs) participated by those diagnosed with COVID-19 and treated with essential oils as adjuvant therapy. Quality assessment was carried out using Cochrane 'risk-of-bias' 2.0 tool. A total of 2112 records were retrieved from the initial screening, which was reduced to four publications (n=344 individuals). The foregoing studies reported that essential oils could improve the recovery rate, alleviate post-COVID-19 fatigue, and prevent disease progression. Regarding their potential antiviral activity, better designed studies are needed. In conclusion, essential oils as adjuvant therapy are beneficial in ameliorating mild COVID-19 symptoms.

Keywords: Volatile compound, aromatherapy, COVID-19, SARS-CoV-2 infection, respiratory tract infection

Introduction

Coronavirus disease 2019 (COVID-19) has been a major concern for global health issues [1]. As of April 5th, 2023, the number of deaths from the COVID-19 pandemic has reached 6,893,190 worldwide with a total of 762,201,169 infection cases [2]. This disease is caused by a positive-sense single-stranded RNA virus – severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [3]. Patients suffering from COVID-19 may experience mild symptoms including fever, cough, headache, and sputum which can progress to more severe conditions including acute respiratory distress syndrome (ARDS) and death [4]. The available antivirals such as remdesivir, nirmatrelvir, and molnupiravir have some benefit in reducing hospitalization and death, but real-world studies suggest a lower efficacy of these drugs over that claimed in the original trials [5,6].

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Previously, researchers have explored the utility of essential oils as antiviral, including against human immunodeficiency virus (HIV) [7] and Middle East respiratory syndrome coronavirus (MERS-CoV) [8]. There is some evidence that essential oils can improve flu symptoms such as fatigue, sputum, fever, and cough [9–12]. Review articles have suggested that essential oils could also be used in managing COVID-19 disease [13, 14]. Several clinical studies have been performed to test the efficacy of essential oils in improving COVID-19-related symptoms [15–17]. Unfortunately, previously published systematic reviews only covered computational or preclinical studies [18,19]. Herein, we performed a systematic review of randomized controlled trials assessing the efficacy of essential oils in COVID-19 management.

Methods

Search strategies

The literature search, screening, and selection process followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), which was performed independently by two reviewers – D.R.R. and A.P. The search was performed on December 7th, 2022, on Scillit, Scopus, SciFinder, and PubMed without restriction on the publication date. The truncation of "essential oils to treat COVID-19" was used, where Boolean operators ('AND' and 'OR') were applied. To be included, the enrolled participants must be infected by SARS-CoV-2 (proven by RT-PCR) or had post-infection symptoms. Studies reported the results of essential oil therapy as adjuvant to standard care were included. Those using unclear compositions of essential oils were not included. Only randomized controlled trials (RCTs) reported in English were included. Review articles, case reports, conference abstracts, patents, commentaries, editorials, and erratum were excluded.

Quality assessment

The quality of the included studies was evaluated by using RoB 2.0: A revised Cochrane risk-of-bias tool for randomized trials, performed by D.R.R. and A.P. independently. The assessment tool has 5 domains, which are: (1) Randomization process; (2) Deviation from intended intervention; (3) Missing outcome data; (4) Measurement of the outcome; and (5) Selection of the reported result. Each domain was marked as 'low risk', 'some concerns', or 'high risk' as the quality indicator.

Data extraction

Number of total participants, age range, and COVID-19 severity were collected as participants' characteristics. We also collected the names of essential oils and their administration method. Outcomes such as viral clearance, symptoms recovery, fatigue level, and adverse effects were recorded. Most of the data were presented narratively, hence no data conversion was applied.

Results

Characteristics of included studies

A total of 2,112 studies were initially identified. By applying the inclusion and exclusion criteria, we obtained 4 studies; two from India, one from the United States, and one from Malaysia. The flow diagram summarizing the selection process is presented in **Figure 1**. During selection, a study performed on healthcare workers who were not infected by SARS-CoV-2 was considered irrelevant, hence being excluded [21]. Studies from Malaysia and India were also excluded because they used essential oils-containing mouthwash but did not specify the essential oils [22–24]. A total of 344 participants were included. Except for Dutt et al. [15] and Khairiah et al. [20], the other 2 studies included a placebo-controlled group [16,17]. The four studies used mixtures of essential oils as an adjunct therapy for symptomatic COVID-19 [15,17] or post-COVID-19 [16]. Details of the characteristics of the included studies are presented in **Table 1**.

Efficacy of essential oil in managing COVID-19

Essential oils were reported to reduce both symptoms of COVID-19 disease [15,17,20] and sequelae [16]. The administration of essential oils as adjuvant could was observed to be more beneficial for mild COVID-19 as compared to moderate severity [15,17]. Improvement in anosmia and dysgeusia was particularly observed in two study [17,20]. However, it is still unclear whether the essential oils could be more beneficial in accelerating viral clearance as compared to the standard care [15,17]. These differences in efficacy could be derived from the heterogenous composition of the essential oils used. Studies have used mixtures of 17–19 different essential oils [15,17]. Among those components, the most commonly used essential oils were eucalyptus, lemon oil, thyme oil, clove oil, and frankincense oil. Routes of administration varied; oral [15] and respiratory [16,17,20]. Regardless, these studies reported no adverse events that could be correlated with essential oils administration, suggesting their safety as therapeutic agents.

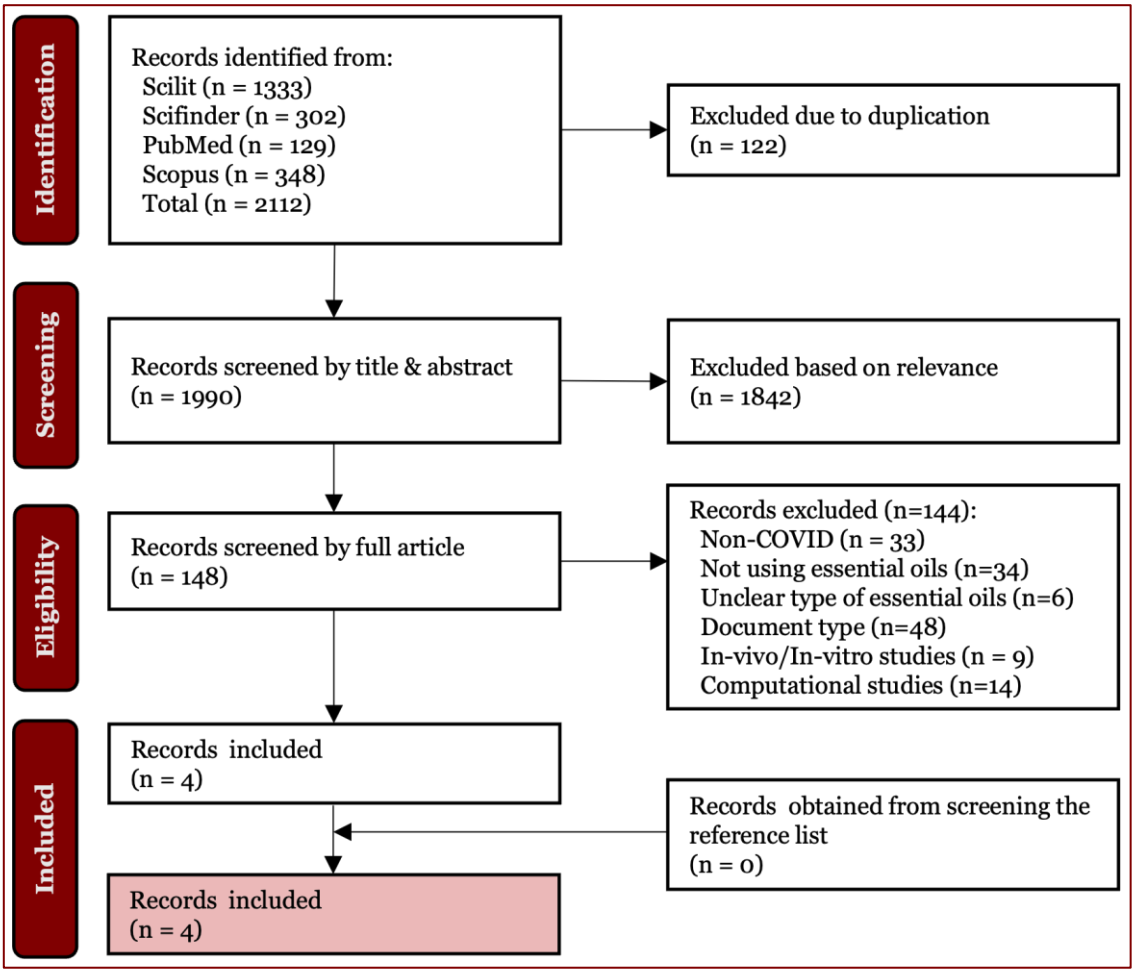

Figure 1. PRISMA flow-chart of the included studies that reported on therapeutic effect of essential oils against COVID-19.

Quality of the included studies

Results from the quality assessment have been presented in **Figure 2**. The included studies were considered to have moderate to high qualities. Among the included studies, two studies were marked with a low risk of bias [16,17] and two studies – some concerns of bias [15,20]. The studies by Dutt et al. [15] and Khairiah et al. [20] had some concerns due to not clearly stating how the blinding was conducted, especially with routine examinations performed during the study. The rest of the other domains were considered as low risk of bias.

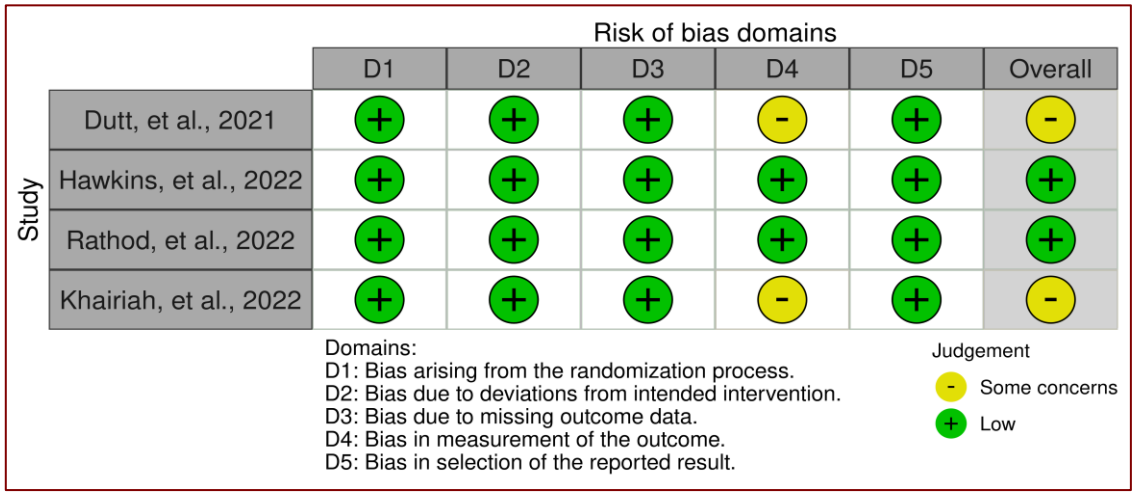

Figure 2. Results from the quality assessment using Cochrane 'risk-of-bias' tool.

Table 1. Characteristics and outcomes of the included studies

Author, Year [Ref]	Country	Participants	Essential oils	Administration	Outcome
Dutt et al., 2021 [15]	India	*n*=60 Age: ≥18 years old Severity: Mild to moderate symptoms.	Oregano oil, clove oil, lemongrass oil, cinnamon oil, neem oil, blackseed oil, spearmint oil, peppermint oil, franckincense oil, lemon oil, eucalyptus oil, coriander oil, lavender oil, rosemary oil, thyme oil, tea tree oil, and sweet orange oil.	Oral	• Rapid viral clearance • Symptomatic recovery • Safe based on serum ferritin, CRP, and NLR
Hawkins et al., 2022 [16]	United States	*n*=40 (female only) Age: 19–49 years old 5–6 months post-COVID-19	Thyme oil, orange peel oil, clove oil, and frankincense oil	Inhalation	• Lowering fatigue • Headache mostly from post-COVID-19 symptoms
Rathod et al., 2022 [17]	India	Phase I *n*=45 Age: 18–55 years old Phase II *n*=99 Aged: 18–65 years old Severity: Asymptomatic or mild	Lemon oil, oregano oil, tea tree oil, java citronella oil, turmeric oil, peppermint oil, lavender oil, ginger oil, frankincense oil, eucalyptus oil, wheat germ oil, basil oil, cedarwood oil, holy basil oil, cinnamon oil, sage oil, and clove oils.	Nebulization	• Reduced the severity progression • Ameliorate anosmia and dysgeusia • Did not affect the viral clearance
Khairiah et al., 2022 [20]	Malaysia	*n*=100 Aged: ≥18 years old Severity: Mild to moderate symptoms	Eucalyptus oil, lemon oil	Inhalation	• Reduce the severity and number of symptoms • No adverse event

CRP, C-Reactive Protein; NLR, Neutrophil Lymphocyte Ratio

Discussion

Administration of essential oils has been found efficacious in preventing both disease progression and better symptomatic recovery after COVID-19 disease [15,17,20]. Faster viral clearance could

be attributed to the antiviral activities of essential oils that have been observed for eucalyptus oil, rosemary oil [25–27], lemon oil, and geranium oil [28]. Some antiviral activities involve the downregulation of angiotensin-converting enzyme II (ACE2) and transmembrane protease serine 2 (TMPRSS2) which act as viral entry points [29]. Several antiviral mechanisms of essential oils have been suggested (**Figure 3**) [19]. The present studies were not able to draw a clear conclusion regarding the antiviral activities of essential oils. Previous studies have suggested that only some essential oils have antiviral activities, and there remains the possibility that other essential oils may actually facilitate viral entry [28,30].

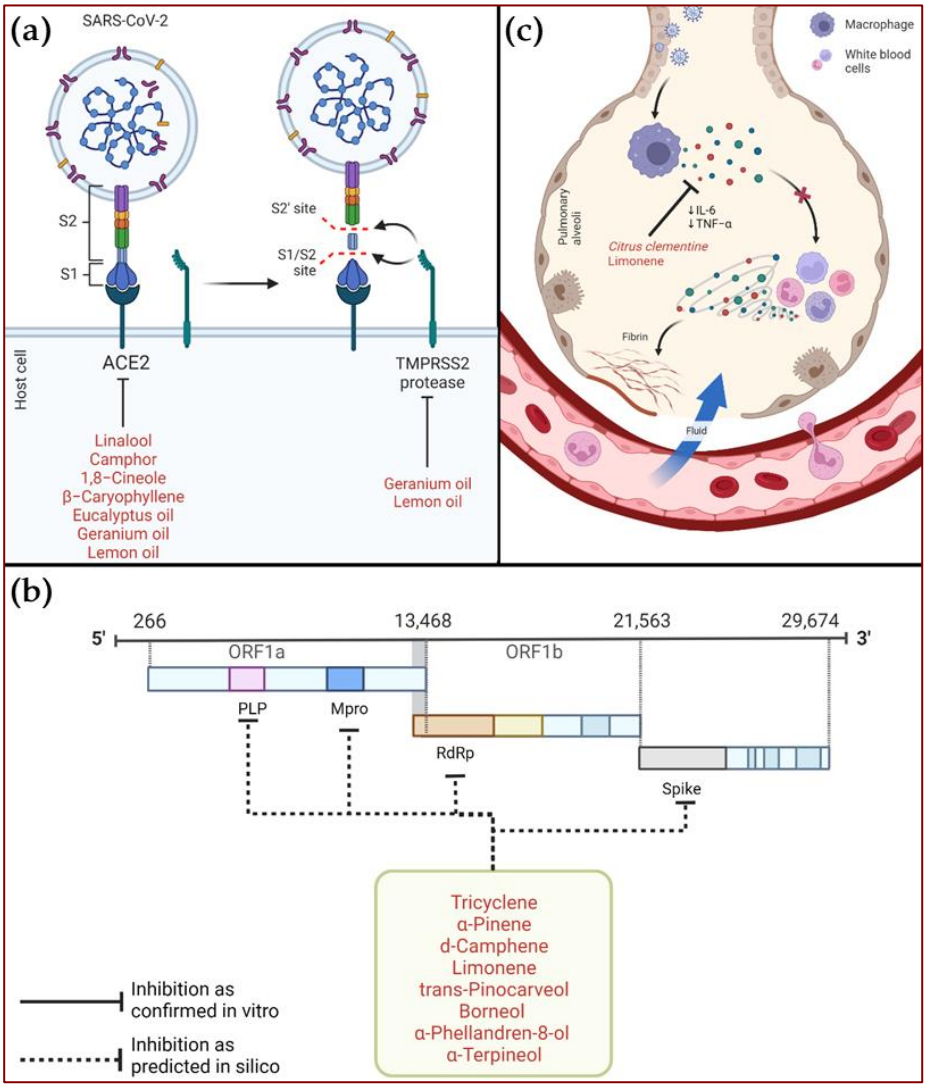

Figure 3. Mechanisms of essential oil in blocking the entry of SARS-CoV-2 (a) and interacting with viral protein (b). Attenuation of SARS-CoV-2-induced pro-inflammatory cytokines release by essential oils (c). Reproduced under the terms of Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/), citing [19].

Though the evidence for an antiviral effect of essential oils is unclear, their efficacy in improving COVID-19 symptoms is better [15,17] including the sequelae of COVID-19 [16]. Patients with COVID-19 disease can develop severe symptoms secondary to the unregulated release of proinflammatory cytokines such as interleukin(IL)-6, IL-7, as well as tumor necrosis factor-α (TNF-α) [31,32]. The long-term impacts of COVID-19 are derived from the alteration of neurotransmitter signaling concomitant to dysregulation of IL-1β, IL-6, IL-4, IL-10, and TNF-α [33]. Eucalyptus oil was found to improve systemic inflammation, without reducing the activities of phagocytic monocytes and macrophages [34]. Essential oils component from orange peel (*Citrus clementine*), limonene, has been shown to normalize levels of TNF-α and IL-6 in SARS-CoV-2-infected huh-7 cells [35].

A factor determining the efficacy of essential oils as an adjunct therapy for COVID-19 management, other than the difference in compositions, is their administration route. Inhalation and nebulization have been used as administration methods for essential oils [16,17]. No adverse effects were reported in these two studies. A study measured serum ferritin, C-reactive protein (CRP), and neutrophil-lymphocyte ratio (NLR) during treatment and concluded that the essential oils were safe [15]. However, a wide variety of bioactive compounds in the essential oils of interest might exert drug interactions that are unclear whether the interaction is antagonistic or synergistic.

Conclusion

Essential oils are efficacious in managing mild COVID-19 symptoms. They may also have the potential to act as anti-SARS-CoV-2 agents. However, the limited sample size and study design limit the interpretation of the direct anti-viral effects of essential oils. The use of essential oil as a mixture, instead of using its single component, further limits the interpretation of the available evidence. We recommend further research using single essential oils such as limonene and eucalyptol to observe whether they interact synergistically or antagonistically.

Ethics approval

Not required.

Acknowledgments

None.

Competing interests

All the authors declare that there are no conflicts of interest.

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Underlying data

All data underlying the results have been presented in this article.

How to cite

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