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Effects of essential oils on symptoms and course (duration and severity) of viral respiratory infections in humans: A rapid review

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BRIEF OVERVIEW

Oral doses of certain essential oils may reduce symptoms of acute respiratory infections of viral origin. It is likely that the commercially available essential oil capsules Myrtol® (a mixture of essential oils of eucalyptus *Eucalyptus globulus*, sweet orange *Citrus sinensis*, myrtle *Myrtus communis* and lemon *Citrus limonum*) and Tavipec® (spike lavender *Lavandula latifolia*) could also provide mild to moderate symptom relief in patients with viral respiratory diseases. Myrtol® may also improve the course (duration and severity) of acute bronchitis of viral origin, in humans. Both products were well tolerated, with most of the mild to moderate side-effects affecting the gastrointestinal tract. This review found no research evidence describing the clinical effect of inhalation of essential oils for acute respiratory viral infections.

VERDICT

Clinical evidence from published clinical trials identified in this rapid review suggests that oral administration of blends of certain essential oils (EO) can reduce symptoms of acute respiratory infections of viral origin in humans, namely acute sinusitis and acute bronchitis.

There is clinical evidence for orally administered *Lavandula latifolia* essential oil (Tavipec®) (n = 2) and a blend of essential oils of *Eucalyptus globulus*, *Citrus sinensis*, *Myrtus communis* and lemon *Citrus limonum* (Myrtol® and its successors GeloMyrtol® and GeloMyrtol® Forte) (n = 3) to reduce symptoms of acute sinusitis and acute bronchitis of viral origin(s) [1–5]. All five clinical trials relied mostly on (subjective) symptom scores to determine the treatment effect. Differences between treatment and placebo symptom scores in these clinical trials were statistically significant, although the differences in absolute numbers were small. Furthermore, clinical evidence suggests that Myrtol® is also able to improve the course (duration and severity) of acute bronchitis of viral origin, in humans [3,5].

No clinical evidence was found on whether EO can also improve symptoms and/or course of other acute respiratory infections, like influenza or acute respiratory distress syndrome caused by viruses of the coronavirus class. Further clinical trials with these and other EO (or blends of EO), and other administration forms, like steam inhalation or personal inhalers, are warranted to further elucidate the potential of commonly available EOs in treating acute respiratory infections of viral origin, especially influenza and COVID-19.

1. Background

Essential oils (EO) are steam-distilled plant extracts containing volatile terpenoids and phenylpropanoid compounds with a molecular weight of less than 300 Daltons. The anti-inflammatory

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and anti-microbial properties, including mode of action (MoA) of EO, have been addressed in numerous pre-clinical (*in-vitro* and *in-vivo*) studies [1]. A recent review [6] of the antibacterial, anti-fungal and antiviral properties of EOs found evidence of *in vitro* anti-viral activity for several virus species, although none for the novel coronavirus (SARS-CoV-2). Although essential oils are often inhaled or applied dermally, they can also be ingested in enteric coated or soft gel capsules. Orally administered EO are thought to be absorbed from the gastrointestinal tract, enter the blood circulation and reach the mucosal secretory glands whereupon they exert their secretolytic effects [1].

2. Search strategy

2.1. Research question

"Can essential oils improve symptoms and course (duration and severity) of acute respiratory infections of viral origin in humans?"

2.2. Inclusion/Exclusion criteria

2.2.1. Inclusion criteria

Studies were included if they reported human prospective intervention studies (randomized controlled trials) in adults (aged 18 years and over) with reported acute viral respiratory infection (where symptoms began in the first 0–5 days prior to inclusion in the trial).

2.2.2. Exclusion criteria

Case studies, case reports, animal studies, *in-vitro* studies, in-silico studies, studies on children only, COPD, asthma, chronic bronchitis, anti-bacterial only, studies on respiratory symptoms without any further clarification about the cause for the symptoms. Studies were excluded if the study population was reported as diagnosed with allergies or chronic respiratory conditions. They were excluded if there was no English abstract.

2.3. Databases

EMBASE-OVID, CINAHL-EBSCO and Web of Science Core Collection and PubMed

2.4. Search terms (example)

All four databases were searched with variations of the following search terms **"1** AND **2** AND 3″.

1 Research articles (Clinical trials, observational and prospective studies), all limited to human *All terms separated with "OR":* Clinical Trial; Clinical Trial, Phase II; Clinical Trial, Phase III; Clinical Trials, Phase I; Controlled clinical trial; Controlled trial; Random Allocation; Randomized controlled; Randomized controlled trial; Single blind method; Double-Blind Method; Multicentre Study; Placebo;
2 Viral respiratory tract infections including coronavirus (and all terms like COVID-19, SARS-CoV-2, MERS-CoV), human influenza and viral pneumonia *All terms separated with "OR":* MERS-CoV; Middle East Respiratory Syndrome Coronavirus; SARS Virus; SARS-CoV; SARS-CoV-1; SARS-CoV-2; 2019-nCoV; coronavirus 2; Coronavirus disease 2019; COVID-19; Novel coronavirus; Severe acute respiratory syndrome; Influenza; Infectious bronchitis virus; Respiratory viral infection; Viral Respiratory Tract Infection; Viral pneumonia; Virus pneumonia;
3 Aromatherapy or essential oils or volatile oils or plant oils as Major Subject Headings *All terms separated with "OR":* Aromatherapy; Essential oil; Oils, Volatile; Eucalyptus Oil; Tea Tree Oil; Cineole; Eucalyptol; Monoterpenes; Terpenes;

As part of our initial searches we identified several reviews on the subject, and retrieved relevant-looking human clinical trial reports from the reference lists, as well as harvesting their key words, MeSH and subject headings.

2.5. Critical appraisal

The risk of bias (RoB) of study findings was assessed using the revised Cochrane RoB tool for randomised trials (RoB 2) https://sites.google.com/site/riskofbiastool/welcome/rob-2-0-tool/current-version-of-rob-2 (see Supplement 2). In the first domain (randomisation process), all trials were rated as low risk of bias [1–5,7,8]. For domain 2 (treatment assignment), all trials were rated as low risk of bias [1–5,7,8]. Under domain 3 (missing outcome data), all trials were rated as low risk of bias [1–5,7,8]. For domain 4 (measure of outcomes), all trials were rated as low risk of bias [1–5,7,8]. In domain 5 (selective reporting), one trial was identified as high risk of bias [2], with the remaining trials rated as having low risk of bias [1,3,2–5,7,8]. Overall, six trials were judged as having low risk of bias [1,3,2–5,7,8], whereas one trial was rated as having some concerns [2]. These judgements should be taken into consideration when interpreting the findings of this review.

3. Results

The database searches identified 265 citations. In total, 29 duplicates were removed leaving 236 citations to be screened. After title and abstract screening, 30 citations were left with 23 citations further excluded based on the pre-defined criteria. The 23 were excluded based on: publication in non-peer-reviewed sources (n = 8); *in-vitro* studies (n = 4); review articles (n = 7); not placebo controlled (n = 2); conference abstract (n = 1); study in Russian with no English abstract (n = 1). The remaining 7 articles underwent extraction (results in Supplement 1) and were included in this rapid review.

3.1. Study design

All seven selected studies were double-blind, placebo-controlled, randomised controlled trials (RCTs) (see Table 1). The EO treatment arms ranged in number of participants from 36 to 196, with similar sized placebo groups, and four out of the seven trials [1,3,4,7] had estimated required sample size. Six out of seven trials were conducted in a primary care clinical setting [1,2,4,5,7,8], and one across multiple ambulatory care centres [3]. Patients were assessed in the clinic, but self-administered the treatments at home (except for the initial throat spray treatment [8]). They also kept patient diaries, completed symptom scales and used manual counters to record incidences of coughing fits in the clinical trials on acute bronchitis. Four of the seven clinical trials were multi-centred [1,3,5,7].

Six out of the seven selected trials were conducted in Europe, three in Germany [2,3,5], two in Austria and Poland [1,4], one in Crete [7]. One trial was conducted in Israel [8].

All included trials defined acute inflammatory respiratory diseases as symptom onset 0–5 days before start of treatment. Three clinical trials examined acute bronchitis [3–5], while others examined acute sinusitis (n = 2) [1,2], and upper respiratory tract infections, most likely of viral origin (n = 2) [7,8]. Fever of >38-39.5 °C was applied as an exclusion criterion during recruitment in three clinical trials to exclude participants with a likely (secondary) bacterial infection [1,3–5].

3.2. Summary of findings

All seven selected clinical trials investigated acute inflammatory respiratory diseases but focused on different respiratory tract infections and used essential oil blends with different composition. Trial characteristics are summarised in Table 1, and results are summarised in Table 2. Except for one clinical trial [8], all clinical trials used orally administered EO capsules. All clinical trials employed subjective symptom scores to analyse the trial outcome [1–5,7,8]. In two of the Myrtol® trials, clinicians also evaluated changes in clinical signs [3,5]. Each clinical trial reported on the effect of the EO treatment on the symptoms as the primary outcome measure.

One trial included a total of 60 participants with upper respiratory tract infections (URTI) diagnosed as pharyngotonsillitis, viral laryngitis, or viral tracheitis [8]. Participants administered a topical spray with a blend of 5 EO directly into their own throats. On the first day of the trial, a total dosage of 42.24 mg (16 sprays) EO was applied over 20 min and during the next 2 days, a daily dose of 52.8 mg of EO was applied. The total duration of this clinical trial was 3 days. The EO spray had immediate beneficial effects on symptom relief compared to placebo ($p = 0.019$) after 20 min but had no statistically significant difference in effect on symptom severity at the end of the 3-day trial. The placebo may not have been physiologically inactive, as it contained a lemon flavour, possibly containing compounds also found in the EO spray.

A trial examined the effect of an orally-administered blend of three EOs from Cretan herbs on individuals (n = 108) presenting with “common cold” symptoms from an upper respiratory tract infection (URTI), within < 24 h onset [7]. Respiratory viruses were detected, in 48/94 (51 %) patients tested. The intervention group were given 13.2 mg EO daily for a total duration of 7 days. The study authors reported no statistically significant results, according to symptom duration or severity between the two treatment arms. There was a statistically non-significant trend towards shortening of the length of the time with severe symptoms in the EO arm.

Two trials employed Tavipec® capsules delivering 900 mg of EO from the flowering tops and stalks of *Lavandula latifolia* (spike lavender) daily [1,4]. One trial examined the effects of Tavipec® on **acute rhinosinusitis** of viral origin with recent onset (within the last 3–5 days) and included 288 participants [1]. A statistically significant lower major symptom score (MSS) in the Tavipec® arm compared to placebo was reported at the end of the treatment (2.52 vs. 3.55, $p = 0.001$; CI_{95}: 0.425; 1.618). Furthermore, the impact of symptoms on QoL was significantly reduced (1.60 vs. 3.04; CI_{95}: 0.98; 1.91) on day 8. A significantly higher proportion of Tavipec® treated patients experienced a reduction in the Sino-Nasal Outcome Test (SNOT-22) symptom scores of $\geq$ 10 points at day 5 or day 8, resulting in final scores of 9.49 vs. 15.03 ($p = 0.002$) in the Tavipec® vs. the placebo arm on day 8.

The clinical trial examining Tavipec® in the treatment of **acute bronchitis** of viral origin with recent onset (within the last 2 days) (n = 269) [4] reported a statistically significant decrease in the bronchitis symptom score (BSS) at day 7 and day 10 for Tavipec® as compared to placebo (4.79 vs. 3.20; $p < 0.005$ for a 25 % difference, respectively 6.47 vs. 4.32; $p < 0.009$ for a 25 % difference). At baseline (day 0) BSS scores were 8.39 for Tavipec® and 8.25 for placebo and reduced to 3.60 vs. 5.05 respectively on day 7 and to 1.92 vs. 3.93 respectively on day 10. Furthermore, most additional signs and symptoms of acute bronchitis (especially of acute cough and chest pain) as well as the patient global quality of life (QoL) improved statistically significantly with Tavipec® as compared to placebo ($p < 0.0001$).

Three clinical trials used Myrtol® capsules - a standardised distillate of a mixture of essential oils of eucalyptus *Eucalyptus globulus*, sweet orange *Citrus sinensis*, myrtle *Myrtus communis* and lemon *Citrus limonum* (66:32:1:1) – resulting in administration of 1200 mg EO daily in the treatment arm [2,3,5]. One trial involved

Table 1
Trial demographics Abbreviations: Upper respiratory tract infection (URTI).

Author date	Country	Condition	Treatment	EO Dose per day/ number of days	Sample size (Total: **treatment**; placebo; comparators
Federspil [1]	Germany	Acute sinusitis	Myrtol[1] standardised capsules (300 mg EO per capsule) Comparable EO (unspecified)	1200 mg/ 6-8 days	330: **109**; 111; 110
Gillissen [2]	Germany	Acute bronchitis onset < 2 days	Myrtol® (GeloMyrtol®® Forte) capsules (300 mg EO per capsule)	1200 mg/ 14 days	398: **196**; 202
Matthys [3]	Germany	Acute bronchitis onset < 5 days	Myrtol®® standardised capsules (300 mg EO per capsule) (comparators cerufoxime & ambroxol)	1200 mg/ 14 days	681: **170**; 172; 171; 163
Duijker [4]	Crete	Upper respiratory tract infections -URTI –51% viral	Blend of 3 Cretan herb[2] essential oils, (52% carvacrol; 12 % eucalyptol) in extra virgin olive oil, capsules	13 mg/ 7 days	105: **54**; 51
Dejaco [5]	Austria & Poland	Acute (rhino-) sinusitis Onset 3-5 days	Tavipec[3] – Spike Lavender (*Lavandula latifolia*) capsules	900 mg/7 days	288: **147**; 141
Kähler [7]	Austria & Poland	Acute bronchitis onset =<2 days	Tavipec®® – Spike Lavender (*Lavandula latifolia*) capsules	900 mg/ 10 days	269: **134**;135
Ben-Arye [8]	Israel	URTI - diagnosed as pharyngotonsillitis, viral laryngitis, or viral tracheitis	Blend of 5 essential oils (3% v/v in Polysorbate 80)[4], throat spray delivering 0.1 ml per spray	42.24 mg (4 sprays x 4 times) over 20 minutes day 1; 52.8 mg (4 sprays x 5) on days 2 and 3	60: **36**; 24 N.B. the placebo was 0.1% of a Lemon VIP additive (Florasynth)

[1] Myrtol standardised to at least 75 mg 1,8-cineole, 75 mg limonene, 20 mg alpha-pinene per 300 mg capsule, taken from oils of Myrtle and Lemon (from product information leaflet).

[2] Three Cretan Herbs - Essential oils of Spanish oregano (*Coridothymus capitatus* (L.) Rchb. f. synonym of *Thymbra capitata* (L.) Cav.); Cretan dittany (*Origanum dictamnus* L.); Sage (*Salvia fruticosa* Mill., *Salvia pomifera* L.) blended in extra virgin olive oil 15 ml/L (a 1.5% v/v blend) ratio not specified.

[3] Tavipec – Spike Lavender (*Lavandula latifolia*). The main components of Spike Lavender are the monoterpenes linalool, 1,8-cineol and camphor in concentrations of 34-50%, 16-39% and 8-16% as sourced from the European Pharmacopoeia (http://online6.edqm.eu/ep800/).

[4] Five essential oils in blend – Lemon Eucalyptus (*Eucalyptus citriodora*), (10%), Eucalyptus Blue Gum (*Eucalyptus globulus*) (20%), Peppermint (*Mentha* × *piperita*) (20%), Syrian Oregano or Za'atar (*Origanum syriacum* L.), (30%) Rosemary (*Rosmarinus officinalis* L.) (20%) dissolved in Polysorbate 80 to give a final concentration of 3% v/v essential oil.

participants (n = 220) with **acute sinusitis** (diagnosed by a clinician) [2], resulting in a greater symptom score reduction after 5–7 days (10.5 Myrtol® vs 9.2 placebo; p = 0.003). There were no differences in the duration of disease between groups.

The two other Myrtol® studies examined its effects on **acute bronchitis** [5,3]. One trial [3] included individuals with onset of bronchitis in the previous five days (n = 342) and found that symptoms regressed in both the Myrtol® and placebo arms but more slowly and less completely in the placebo arm. Acute bronchitis regressed faster and more completely by end of study (day 14) in the treatment arm (Myrtol® = 92.9 % responders, Placebo = 77.3 % responders, $p < 0.001$). The rate of deterioration of acute bronchitis resulting in study discontinuation was higher in the placebo group compared to the Myrtol® (11 % (CI_{95} 6.8 – 16.7) vs 1.2 % (CI_{95} 0.1–4.2). Joint pain, headache or abnormal auscultation, reduction in coughing fits, and difficulty in coughing up sputum, and an increase in the participants' reported general wellbeing (QoL) were also positively influenced by Myrtol® although statistical significance was not reported. The second study of Myrtol® in the treatment of acute bronchitis recruited individuals reporting onset of symptoms in the previous two days (n = 398) [5]. At the end of the trial there was a greater difference in the reduction in the mean number of day-time coughing fits on day 7–9 in the GeloMyrtol® Forte arm compared to placebo (62.1 % vs. 49.8 %; $p < 0.001$). There were also statistically significantly less night-time coughing fits, less difficulty coughing up sputum, less sleep disturbance due to night-time coughing in the treatment arm. Furthermore, with GeloMyrtol® Forte, the median time to 50 % reduction in coughing fits was statistically significantly shorter 5–6 days vs 6–8 days for placebo (p = 0.0002) and there were more patients without day-time coughing fits.

3.3. Adverse effects

All six clinical trials using orally administered EOs reported mild adverse effects (AEs) likely to be due to EO treatment, which were mainly gastrointestinal symptoms [1–5,7]. Adverse events reported from using the throat spray [8] were mild symptoms of dry pharynx and slight stinging sensations, although the number of people experiencing these symptoms was not reported.

The number of reported AEs in the Myrtol® vs placebo arms were 7.9 % vs 7.6 % [3], 15.9 % vs 16.3 % [5], 11 % vs 7.2 % [2]. The number of reported AEs in the Tavipec vs placebo arms were 17.6 % vs 5.7 % [1] and 9.2 % vs 3.2 %.

All EO treatments were considered tolerable and the predominant adverse effects were mainly mild and transient gastrointestinal effects.

3.4. Clinical significance

The two clinical trials on upper respiratory tract infections (URTI) using the throat spray [8] and the blend of Cretan herb essential oils [7] showed little clinical efficacy in ameliorating the duration and severity of symptoms of the different underlying diseases, upon the treatment with essential oils (EO). The two clinical trials on Tavipec® [1,4] suggested clinical efficacy of Tavipec® in the reduction of severity of symptoms of acute sinusitis and acute bronchitis, but not reduction in duration of symptoms. Patient QoL also improved significantly with Tavipec® compared to placebo [4]. The three clinical trials on Myrtol® capsules [2,3,5] suggested clinical efficacy of Myrtol® capsules in the reduction in severity and duration of symptoms of acute sinusitis and acute bronchitis and improvements in participants' quality of life [2,3,5].

4. Disclaimer

This article should not replace individual clinical judgement. The views expressed in this rapid review are the views of the authors and not necessarily from the host institutions. The views are not a substitute for professional medical advice.

5. Author contributions

The search was created by TA, SP and EJB, and conducted by EJB and GC. Citations were screened by title and abstract by KB and SP. The full texts of remaining citations were accessed and screened by by SP and EJB. Data were extracted from retained articles by EJB and SP. The rapid review was drafted by SP and EJB. All authors reviewed and approved the final version.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.aimed.2020.07.005.

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