



#### A continuous publication, open access, peer-reviewed journal

ACCESS ONLINE

#### REVIEW

#### Aromatic ointments for the common cold: what does the science say?

#### Andrew Smith<sup>1</sup>, Oliver Matthews<sup>2</sup>

<sup>1</sup>School of Psychology, Cardiff University, Cardiff, UK; <sup>2</sup>Procter and Gamble UK, Weybridge, Surrey, UK

#### Abstract

**Background:** Upper respiratory tract infections occur with an annual incidence of 17.2 billion cases globally. The negative impact that symptoms have on sleep is thought to slow the recovery process. Plant-derived aromatics have been used since ancient times to treat respiratory illnesses. In this narrative review, we summarize the use of aromatics for the symptomatic relief of upper respiratory tract infections and how this affects sleep quality.

**Methods:** Literature searches were conducted using a series of search terms and results were screened for relevance. Additional references were included according to the expert knowledge of the authors.

**Discussion:** Multiple studies have observed that essential oil mixtures of aromatics enhance symptom relief for upper respiratory tract infections and their inhalation has been reported to have antitussive effects. Clinical trials assessing the efficacy of an ointment containing menthol, eucalyptus and camphor found patients to experience faster nasal

cooling and decongestion times. Treatment with the same ointment also resulted in significant improvements in reported sleep quality. Aromatic treatment did not improve objective nasal airway measures in any of the studies.

**Conclusion:** Whilst not affecting objective measures of nasal airway resistance, the use of aromatics leads to improvements in a number of subjective sensations associated with the common cold. Such benefits result in better sleep, which likely aids recovery. Therefore, aromatics remain a well tolerated and effective option for the symptomatic relief of upper respiratory tract infections.

**Keywords:** aromatic, common cold, cough, menthol, nasal congestion.

#### Citation

Smith A, Matthews O. Aromatic ointments for the common cold: what does the science say? *Drugs Context*. 2022;11:2022-5-6. https://doi.org/10.7573/dic.2022-5-6

## Introduction

Common colds are the most prevalent human infectious disease<sup>1,2</sup> and are caused by viral upper respiratory tract infections (URTIs). Infection is established in the epithelial mucosa and affects the nose, nasopharynx and paranasal sinuses.<sup>3</sup> Although generally a mild illness, the combination of bothersome symptoms and loss of sleep can lead to time off sick from work for adults, who may experience two to four colds a year, and time off school for children who may experience as many as six to eight colds a year.<sup>2</sup> In addition, parents' sleep can be substantially disrupted by the need to attend to the symptoms of their children during the night, which can also lead to time off work. Globally, the incidence cases of URTIs reached 17.2 billion in 2019,<sup>4</sup> whilst in the United States alone, approximately 20 million working days and 22 million school days are lost each year due to the common cold.<sup>2</sup> The common cold presents with a range of symptoms

so familiar to sufferers that it is readily self-diagnosed, and most cases never seek medical assistance. Despite this, family doctors handle approximately 25 million visits from people with uncomplicated URTIs each year in the United States.<sup>2</sup> Cold symptoms usually begin with localized manifestations, such as sneezing, followed by headache and sore throat, along with systemic symptoms such as chilliness.<sup>5</sup> In the later stages, symptoms include nasal obstruction, nasal discharge, cough and malaise.

Herbs have commonly been used for the alleviation of respiratory ailments for thousands of years in many regions of the world, including the Mediterranean Basin and the Middle East.<sup>6</sup> The use of herbal essential oils has been empirically based on the weight of evidence for the treatment of symptoms, even before the existence of scientific data. Aromatics derived from five plants, in particular, have been used since ancient times for the feeling of improved

breathing that they produce. These are *Eucalyptus citriodora* and *Eucalyptus globulus*, both of which contain the aromatic citronellal; *Mentha piperita* (peppermint), which contains the active ingredient menthol; *Origanum syriacum*, which contains the active ingredients thymol and carvacrol; and *Rosmarinus officinalis*, which contains camphor and cineol. Today, the usefulness of aromatics for therapeutic purposes has been studied in well-conducted and controlled scientific and clinical studies, which are described in this narrative review.

Whilst aromatic herbs have long been used as traditional remedies and possess broad-spectrum pharmacological activities, with various reports of their microbicidal properties, the focus of this narrative review is on the utility of aromatics for symptomatic relief from the troublesome effects of URTIs and their impact on sleep quality, which aids competent immune function.<sup>7-9</sup> We will present and discuss the data currently available on the efficacy of aromatics for the treatment of the symptoms of URTIs, including randomized blinded clinical trials, after first considering the physiological mechanisms that underlie the symptoms of cold and flu.

## **Methods**

Literature searches were performed using the search terms: "menthol AND aromatic", "camphor AND aromatic", "eucalyptus AND aromatic" and "vapour rub". Results were screened for relevance. References that described antimicrobial effects, administration of systemic treatment or other inappropriate preparations, or treatments other than symptom relief were excluded from the results. Additional references were included according to the expert knowledge of the authors.

## Review

## Physiology of the common cold

Whilst common colds can be caused by any of about 200 different strains of respiratory viruses,<sup>10</sup> the most common causative viruses, which account for up to 50% of symptomatic infections, are Rhinoviruses.<sup>1</sup> The principal symptoms of common cold include nasal congestion, nasal discharge, sneezing, headache, sore throat and cough.<sup>11</sup> During the first 7 days of a cold, the most troublesome symptoms are reported as nasal congestion and cough.<sup>12</sup>

The symptoms of both the common cold and flu are caused by antiviral immune responses<sup>13,14</sup> and are driven by a mixture of proinflammatory cytokines as well as other inflammatory mediators.<sup>15</sup> Whilst cytokines drive systemic symptoms such as fever,<sup>16</sup> other inflammatory mediators, in particular bradykinin, play a pivotal role in the generation of localized symptoms, including sore throat and nasal congestion.<sup>17,18</sup> Thus, the pathophysiological mechanisms that give rise to the symptoms of the common cold comprise two pathways: cytokinedriven systemic symptoms and local symptoms driven by inflammation of the mucosal epithelium in the infected airway.<sup>19</sup>

One of the principal immune cells responsible for initiating the immune response against viral infection is the macrophage, which recognizes pathogen-associated molecular patterns, for example, double-stranded RNA, through specialized pattern recognition receptors, including Toll-like receptors. Upon ligation by molecules from the pathogen, these receptors trigger the production of proinflammatory cytokines,<sup>20</sup> which recruit other immune cells, triggering an inflammatory response. Inflammatory cytokines, including IL-1, tumour necrosis factor (TNF) and the interferons, act on the central nervous system, joints and muscles to produce systemic symptoms such as fever, myalgia, headache, fatigue, loss of appetite, and mood change.<sup>21</sup> In contrast, cellular damage that results from a viral infection of the respiratory epithelium induces the activation of enzymes that stimulate the production of bradykinins and prostaglandins. These, in turn, act on nerves, blood vessels and glands, causing the localized symptoms of sneezing, rhinorrhoea, nasal congestion, cough and sore throat.

The sensations of symptoms of the common cold, including pain, pressure and irritation, are dependent on the cranial nerves that supply sensation to the nose and throat, in particular the maxillary and ophthalmic branches of the trigeminal nerves.<sup>15</sup>

#### Local symptoms

Sore throat likely results from local production of bradykinin and prostaglandins in the respiratory epithelium following infection and is sensed by the cranial nerves that supply the nasopharynx and pharynx. The symptoms of rhinitis and sore throat can be experimentally induced with intranasal administration of bradykinin<sup>17,22</sup> and are enhanced by the presence of prostaglandins.<sup>23</sup> Aspirin and paracetamol are both effective treatments for sore throat and are both prostaglandin inhibitors.<sup>24</sup>

Sneezing is controlled by the sneeze centre in the brainstem and follows stimulation of the trigeminal nerves by inflammation in the nose and nasopharynx. The sneeze centre then activates respiratory muscles and triggers the reflex activation of motor and parasympathetic branches of the facial nerves. Local production of histamine may play a critical role in generating sneezing, as the trigeminal nerves express histamine receptors, and the intranasal administration of histamine causes sneezing.<sup>25</sup>

Rhinorrhoea or 'runny nose' is an early symptom that is associated with sneezing and the reflex activation of parasympathetic nerves that stimulate glandular secretions through nasal ducts into the anterior of the nose.<sup>26</sup> Secretions from nasal and lacrimal glands contribute to nasal discharge and can involve plasma exudates from capillaries as well as elements from both goblet and plasma cells, each of which provides varying contributions according to the

## stage of infection and severity of the inflammatory response.<sup>26</sup>

Nasal blood vessel congestion can cause a blocked nose, a later symptom of colds that increases in severity within the first week from symptom onset.<sup>5</sup> Large capacitance veins are 'erectile' and can dilate, particularly at the anterior end of the inferior turbinate and nasal septum.<sup>27</sup> Nasal resistance to airflow is regulated by swelling in this narrow 'nasal valve' region and is controlled by the sympathetic nerves,<sup>28,29</sup> which can release the potent blood vessel constrictor noradrenaline (norepinephrine) to reverse swelling.<sup>30</sup> Nasal congestion as a result of swelling can lead to a blocked nose when combined with the secretion of viscous nasal mucus, and may even lead to total nasal obstruction in the narrowed airway. Therapeutic decongestion of the nose can be achieved by administration of sympathomimetics such as xylometazaline,<sup>31</sup> oxymetazoline<sup>32</sup> or pseudoephedrine,<sup>33</sup> which constrict nasal erectile tissue.

Measurements of nasal airway resistance are determined, in part, by the minimum cross-sectional area of the nasal valve region. These objective measurements are frequently inconsistent with subjective sensations of nasal obstruction, which occur because the subjective sensation of obstruction is influenced by factors such as air temperature, stimulation of cold receptors in the airway and the feeling of pressure on the congested side of the nose.<sup>34</sup> Furthermore, sensations of obstruction can be caused by nasal congestion in the ethmoid area, ostia of paranasal sinuses and eustachian tube, all of which are distal to the nasal valve and bear no relationship to any changes in nasal airway resistance. Sinus pain may result from changes in the pressure of the sinus air space or in sinus blood vessels.<sup>35</sup> Local production of bradykinin may also cause sinus pain by stimulating pain nerve endings or causing distension of blood vessels in the sinus.<sup>36</sup>

One of the most obtrusive symptoms of the common cold, which can lead to sleep deprivation, thereby reducing immune function, is a dry cough. The cough reflex is controlled from the medulla region of the brainstem<sup>37–39</sup> and can be triggered by stimulation in either the upper (larynx and trachea) or lower airways (bronchi and bronchioles). Unproductive coughs have no useful function and are likely to be caused by inflammation in the nose and throat that spreads to the larynx and trachea, where bradykinin and prostaglandins stimulate airway sensory nerve endings.<sup>40,41</sup> If infection and inflammation continue to spread to the lower airways, they may cause mucus production and expectoration, which can lead to a productive cough later in the course of the cold.

#### Systemic symptoms

The feeling of having a chill is likely to be a central effect due to inflammatory cytokines, such as IL-1 and IL-6,<sup>42</sup> acting on the hypothalamus.<sup>43</sup> Although common colds in adults are not usually associated with fever, a chill can be the initial stage of fever as skin vasoconstricts, causing raised body temperature and shivering. In general, adults tend not to develop fevers

during infection with cold viruses as fever is more common during a primary immune response, and the immune systems of most adults will previously have been exposed to a diversity of cold virus antigens. In infants, this is not the case, and fever occurs more frequently during colds.

Myalgia is common in about 50% of patients with common cold<sup>24</sup> and is caused by cytokines such as TNF, which promotes the breakdown of skeletal muscle<sup>44,45</sup> to release protein stores needed for the production of antibodies.<sup>44</sup>

Together, the symptoms of the common cold can affect the quality of sleep, which is likely to have a detrimental impact on the effectiveness of immunity to infection.<sup>46</sup> Both cough and nasal congestion are recognized as significant impediments to restful and restorative sleep.<sup>47-49</sup> Whilst objective measurements of sleep disturbance are modest, with an average decrease in sleep of approximately 23 minutes and a 5% reduction in sleep efficiency,<sup>50</sup> loss of sleep caused by cold symptoms is generally considered to be clinically meaningful. Sleep parameters correlate with symptom scores, indicating a relationship between sleep disturbance and increasing symptom severity.<sup>46</sup> This correlation is significantly driven by the severity of nasal congestion. Therefore, therapies that alleviate rhinitis without the use of sedation are likely to play an important role in aiding undisturbed sleep, which supports competent immunity.

#### Benefits of subjective relief

Restful and restorative sleep is an important means of enabling the body to fight off infection with cold and flu viruses. Sleep deprivation is reported to cause impaired lymphocyte proliferation and leads to phenotypic alterations in both lymphocytes and monocytes that are likely to impair their function.<sup>7,8</sup> In addition, sustained loss of sleep (<6 hours sleep per night) is associated with an increased risk of viral and bacterial URTIs.<sup>7,9</sup> Therefore, there is a clinical consensus that adequate restful sleep can hasten the healing process and reduce the time to full recovery.

Whilst many of the symptoms of the common cold may aggravate the ease and comfort of sleep, the greatest impact on sleep is likely to be due to nasal congestion and cough.<sup>47–49</sup> Therapeutic relief of nasal congestion and cough is therefore expected to improve sleep quality. Whilst well-established symptomatic relief treatments such as pseudoephedrine, dextromethorphan, paracetamol and codeine act centrally, topical or inhaled aromatic applications, such as menthol, act on local airways improving the subjective sensation of airflow and, in addition, have antitussive effects.<sup>51</sup>

Objective measurements of nasal airway resistance do not correlate with subjective sensations of nasal obstruction. The subjective sensation of nasal obstruction is influenced by factors that are not related to nasal airway resistance, including air temperature, stimulation of nasal cold receptors and the sensation of pressure.<sup>34</sup> This means that the patient

may feel that they can breathe more easily, even whilst there are no objective measures of improved airway patency. It is important to note that, in terms of the patient experience, there is no discernible difference between objective and subjective relief.

Nasal airflow 'cold air' receptors have an important influence on the sensation of nasal patency and patient comfort, as a lack of sensation of nasal airflow causes the perception of stuffiness, even when nasal airflow resistance is within the normal range.<sup>52</sup> As early as 1951, Hensel and Zotterman ascribed the cooling sensation experienced following administration of menthol to the stimulation of cold receptor nerve endings.<sup>53</sup> The reflex effects of nasal airflow on nasal electromyographic activity are enhanced by inhalation of menthol, which may be explained by sensitization of nasal airflow receptors. Therefore, stimulation or sensitization of nasal airflow receptors by aromatics, such as menthol, eucalyptus or camphor, may increase receptor signalling at any given air flow rate.

Nasal airflow receptors also play an important role in the regulation of respiration and influence the timing of breath holds as the onset of involuntary inspiratory muscle contractions can be delayed by cool air circulating through the nose.<sup>54</sup> Application of local anaesthetics to the nose can cause increases in sleep apnoea and upper airway obstruction, suggesting that nasal airflow receptors are important in maintaining the rhythm of respiration during sleep.<sup>55</sup>

Inhalation of menthol has been reported to reduce the frequency of coughing,<sup>51</sup> whilst the inhalation of combined preparations of menthol, camphor and eucalyptus can relieve nasal congestion.<sup>56,57</sup> These effects are considered to be due to the aromatics stimulating thermosensitive, calcium-selective 'transient receptor potential' (TRP) ion channels, that act as 'cold air' receptors. Respiratory virus infection may lead to increased expression of transient receptor potential receptors TRPM8, TRPV1 and TRPA1.<sup>58,59</sup> The cooling sensation associated with menthol and eucalyptus oil is mediated by TRPM8,<sup>60,61</sup> making this receptor the primary candidate for the sensation of nasal decongestion associated with menthol and eucalyptus oil.<sup>62</sup> The TRPV1 and TRPA1 receptors, which are expressed in the larynx and involved in triggering cough,<sup>58,59</sup> interact with menthol, eucalyptus oil and camphor,<sup>63–65</sup> suggesting they may have a role in the mitigation of cough sensitivity reported for these aromatics.

Whilst inhalation of aromatics has not been found to have any impact on objective measurements of inspiratory or expiratory nasal airflow resistance,<sup>56,66</sup> the subjective sensation of improved nasal airflow following inhalation of aromatics is considered to be due to signalling through airway cold receptors. This subjective component of symptomatic relief during the common cold, which from the patient's point of view is just as important as objective relief, is likely to play an important therapeutic role, leading to improvements in selfreported sleep quality and patient comfort,<sup>57</sup> which in turn facilitate more effective immunity against infection.

# The clinical experience of aromatic products for the common cold

Whilst most studies investigating the effects of aromatics on URTIs have assessed either pharmaceutical preparations containing a combination of aromatics, notably menthol, eucalyptus oil and camphor, or sprays containing mixed essential oils, there have been a small number of investigations into the application of a single aromatic in isolation, namely menthol.

A number of therapeutic preparations sold for the relief of cold symptoms include the volatile aromatic compound menthol, which is derived from various species of mint, including peppermint (*Mentha piperita*) and wild mint (*Mentha arvensis*) or can be produced synthetically.

In healthy volunteers with no symptoms, inhaled menthol has no impact on the objective determinations of airway resistance: respiratory frequency, minute ventilation, total inspiratory time/total breath time, or upper airway resistance compared with a sham (air) inhalation.<sup>67</sup> In contrast, a study that modelled cough in healthy subjects by induction of inhaled citric acid found menthol dissolved in eucalyptus oil to be a highly effective antitussive agent. Menthol was administered 55 minutes after cough induction, five times at hourly intervals on three consecutive days, and resulted in a significant reduction in cough frequency at all time points, compared with the pine oil control.<sup>51</sup>

The citric acid aerosol cough model was also utilized in a singleblind study by Packman et al. to assess the antitussive effects of a range of individual aromatic compounds, as well as some combined preparations, by inhalation.<sup>68</sup> Comparisons were made between an ointment containing menthol, camphor, oil of eucalyptus, oil of turpentine, cedar leaf oil, myristica oil and thymol, and each ingredient separately in a petrolatum base, alongside the petrolatum base alone, which were each rubbed into the chest in a single 7.5-g dose for 10–15 seconds. There were significant reductions in citric acid-induced cough compared to baseline for the ointment and individual component formulations of menthol, camphor and oil of eucalyptus.

The effects of mixed essential oils derived from *Eucalyptus citriodora* (citronellal), *Eucalyptus globulus* (citronellal), *M. piperita* (menthol), *Origanum syriacum* (thymol and carvacrol) and *Rosmarinus officinalis* (camphor and cineol) were assessed in patients with URTIs.<sup>69</sup> The essential oil or a placebo spray were administered five times daily for 3 days. Patients' selfreporting of their most debilitating symptom out of sore throat, hoarseness or cough revealed a significant improvement 20 minutes after application of the essential oil spray compared with placebo, though this effect was not sustained at 3 days.

A number of studies have assessed the effects of the combined aromatics commonly used in proprietary aromatic ointments. A mixture of aromatics (menthol, camphor, oil of pine needles and methyl salicylate) was used to treat nasal stuffiness in 36 otherwise healthy volunteers using a visual numerical scale for the subjective assessment of nasal sensation of airflow.<sup>56</sup> Objective measurements of nasal resistance and subjective scoring of nasal sensation of airflow were compared before and after inhalation of a neutral control, vanilla, or the mixture of aromatics. The resistance to airflow in the nasal passage was measured using a nasal resistance meter. Whilst no effect was seen on the objective measures of inspiratory or expiratory resistance, subjective increases in the nasal sensation of airflow were reported by 72% of individuals following inhalation of the aromatic mix, which was highly significant compared with the vanilla control (p<0.01).

A postmarketing observational study assessed the effect of a pharmaceutical aromatic ointment containing camphor, eucalyptus oil, menthol, Norway spruce oil, pumilio pine oil and turpentine oil applied by inunction or inhalation.<sup>70</sup> Data were collected on the application of the ointment in 3060 adolescents who were suffering from colds, acute or chronic bronchitis, bronchial catarrh, or hoarseness. Participants took part in the study for a mean of  $8.0\pm 3.4$  days. The tolerability of the ointment was rated as excellent or good by more than 95% of physicians and patients, with 88% of both physicians and patients judging the treatment effect as mostly excellent or good.

Three clinical trials assessed the effects of a different pharmaceutical aromatic ointment that contains a combination of levomenthol (2.75% w/w), eucalyptus oil (1.5% w/w), turpentine oil (5% w/w) and camphor (5% w/w) as active ingredients, and thymol, cedarwood oil and a soft white paraffin (petrolatum) base as excipients. A partially doubleblinded randomized clinical study assessed whether a single application of the aromatic ointment or petrolatum base was superior to no treatment for nocturnal cough, congestion and sleep difficulty caused by URTI in 138 children aged 2–11 years.<sup>71</sup> Parents applied the aromatic ointment or petrolatum ointment to their child's chest and neck at bedtime and were asked to complete surveys before and after treatment.

There were significantly different improvements in cough, congestion, child and parent sleep difficulty, and combined symptom score between treatment groups, with the aromatic consistently performing the best (p<0.05). No improvements were seen for the severity of rhinorrhoea. In pairwise comparisons, the aromatic ointment was superior to no treatment for cough severity (p<0.01), cough frequency (p<0.01) and nasal congestion (p<0.05), with the most profound effects observed for sleep-related outcomes. Children treated with the aromatic ointment were significantly more able to sleep than were children treated with petrolatum (p<0.01) or no treatment (p<0.01). A notable effect of this that should not be overlooked was a better ability to sleep for the parents of children treated with the aromatic ointment compared with parents of children who received petrolatum (p<0.01) or no treatment (p<0.01).

A randomized, single-blind (investigator), controlled, two-arm, parallel design pilot study assessing an aromatic ointment

containing levomenthol, eucalyptus oil and camphor versus petrolatum was conducted to detect the sensation of nasal cooling and nasal decongestion in 50 otherwise healthy adult patients who were suffering from common cold with nasal congestion.<sup>62</sup> There was a significantly faster time to the first sensation of nasal cooling for patients who received the ointment compared with control (p<0.01), which remained statistically significant at all times from 12 seconds to 15 minutes after application of the product. Furthermore, the time to the first sensation of nasal decongestion was also significantly faster for patients who received the ointment compared to control (p<0.05), which remained statistically significant at all times from 62 seconds to 15 minutes after application of the product.

A randomized, single-blind, controlled, two-arm, parallel design exploratory study of the effects of the same aromatic ointment preparation versus petrolatum on symptom-associated sleep disturbances was conducted in 100 patients with the common cold.<sup>57</sup> Subjective and objective measurements of sleep parameters were assessed, and the primary efficacy variable was subjective sleep quality measured with the Subjective Quality of Sleep Questionnaire (SQSQ). Other measures assessed were ease of falling asleep and depth of sleep (measured with a postsleep visual analogue scale), total sleep time, sleep onset latency, activity score, percentage of sleep, sleep efficiency (measured with actigraphy and SQSQ) and sleep quality index measured with a modified Karolinska Sleep Diary (KSD). There was a statistically significant change from baseline following treatment with the ointment for the primary endpoint question "How was the quality of your sleep last night?" (p<0.05), compared with the application of petrolatum. There were also statistically significant changes from baseline for the ointment compared with petrolatum for the SQSQ question "How refreshed did you feel upon waking up?" (p<0.05), and the KSD questions, "Did you get enough sleep?" (p<0.05), "How was it to get up?" (p<0.05) and "Do you feel well rested?" (p<0.05). There were no statistically significant changes in the objective actigraphy endpoints.

In summary, aromatic ointments containing levomenthol, eucalyptus oil and camphor applied before going to bed can reduce nocturnal cough, subjective sensations of nasal congestion and, importantly, subjective sleep disturbances associated with the common cold.

## Discussion

Aromatics have been assessed for their ability to alleviate the symptoms of URTIs and aid restful sleep in a variety of studies, occasionally as single agents though mostly in combination mixtures and aromatic ointments. Menthol stands out as the aromatic compound of most interest, both because it has been investigated as a single agent and because it has a defined mechanism of action. Menthol is thought to act by signalling through the respiratory airway TRPM8 receptor, which senses cold air.<sup>60,61</sup> This mechanism may explain why menthol creates a sensation of eased nasal breathing, even though airflow is objectively unchanged. A similar mechanism may be considered for the interaction of menthol, eucalyptus and camphor with TRPV1 and TRPA1, which are involved in the cough response.<sup>63–65</sup>

Studies have been conducted that assessed the effects of various aromatics, namely camphor, oil of eucalyptus, oil of turpentine, cedar leaf oil, myristica oil and thymol, as single agents in only one study or in combination with menthol in a number of others. Menthol has been reported to have antitussive effects in induced cough models<sup>51,68</sup> and in children with cold-associated nocturnal cough.<sup>71</sup> In addition, proprietary preparations of aromatic ointments that contain menthol, eucalyptus oil and camphor have been assessed in well-conducted clinical trials, demonstrating clear beneficial effects in the alleviation of localized cold symptoms, including the sensation of nasal congestion, nocturnal cough and cold-associated associated sleep difficulties, whilst having no impact on objective measurements.<sup>57,62,71</sup>

The clinical studies reported by Paul et al.<sup>71</sup> and Santhi et al.<sup>57</sup> suggest a potentially considerable benefit of ointments containing menthol, eucalyptus and camphor on perceived improvement in sleep quality. A restful sleep is an important element in immune competence and resistance against URTIs,<sup>7–9</sup> and the potential importance of the effect of aromatic ointments on sleep quality should not be underestimated.

A variety of over-the-counter ointments containing menthol, eucalyptus oil and camphor are available to patients and may be recommended by pharmacists for the symptomatic relief of nocturnal cough, congestion and sleep difficulty caused by colds. Patient hesitancy towards non-prescription treatments and the potential stigma that aromatic ointments are a 'herbal remedy' may lead some patients to disregard them as an option. Despite this, aromatic ointments may be an especially valuable aid, particularly for those in whom stronger cold relief ingredients, such as paracetamol, pseudoephedrine, dextromethorphan and promethazine, may be contraindicated as well as in children, thus enabling a more restful sleep for both children and their parents.<sup>57,71</sup>

## Conclusion

The symptoms of the common cold, in particular nasal congestion, can adversely affect the quality of sleep, which is likely to delay the recovery time from infection.<sup>46</sup> Importantly, the subjective sensation of nasal obstruction is not related to nasal airway resistance as the sensation of nasal obstruction is influenced by air temperature, stimulation of nasal cold receptors and the sensation of pressure.<sup>34</sup> A number of studies reported in the scientific literature, including controlled clinical trials, provide well-conducted, peer-reviewed evidence for the mechanisms of action and beneficial effects of aromatic ointments in the relief of common cold symptoms. Inhaled aromatics that contain menthol, eucalyptus and/or camphor can ease the subjective sensation of airflow by acting on local airways via the calcium-selective ion channel transient receptor potential 'cold air' receptors such as TRPM8, which interacts with menthol.<sup>60,61</sup> In addition to easing the sensation of nasal airflow, menthol also has antitussive effects.<sup>51</sup> Aromatic ointments containing menthol, eucalyptus and/or camphor can be effective treatments for the symptoms of the common cold, thereby enabling more refreshing sleep, which can speed up recovery.<sup>7</sup> Therefore, aromatic ointments should not be overlooked by pharmacists as an option for any patient with cold symptoms, in particular for children or those in whom stronger medications are contraindicated.

**Contributions:** OM conceived and managed the preparation of the manuscript, conducted literature reviews and helped with the preparation of the manuscript. AS contributed to the preparation, reviewing and the scientific development of the manuscript. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

**Disclosure and potential conflicts of interest:** OM is an employee of Procter and Gamble UK, who produce and market Vicks VapoRub. The International Committee of Medical Journal Editors (ICMJE) Potential Conflicts of Interests form for the authors is available for download at: https://www.drugsincontext.com/wp-content/uploads/2022/07/dic.2022-5-6-COI.pdf

**Acknowledgements:** Medical writing support was provided by Dr Gareth AD Hardy of Niche Science and Technology Ltd, Richmond-upon-Thames, Surrey, UK; this was paid for by Procter and Gamble UK.

Funding declaration: Production of this manuscript was conceptualized, funded and managed by Procter and Gamble UK.

**Copyright:** Copyright © 2022 Smith A, Matthews O. Published by *Drugs in Context* under Creative Commons License Deed CC BY NC ND 4.0, which allows anyone to copy, distribute, and transmit the article provided it is properly attributed in the manner specified below. No commercial use without permission.

**Correct attribution:** Copyright © 2022 Smith A, Matthews O. https://doi.org/10.7573/dic.2022-5-6. Published by *Drugs in Context* under Creative Commons License Deed CC BY NC ND 4.0.

Article URL: https://www.drugsincontext.com/aromatic-ointments-for-the-common-cold-what-does-the-science-say

Correspondence: Andrew Smith; School of Psychology, Cardiff University, 63 Park Place, Cardiff, CF10 3AS, UK. Email: smithap@cardiff.ac.uk

Provenance: Submitted; externally peer reviewed.

Submitted: 31 May 2022; Accepted: 29 June 2022; Publication date: 1 August 2022.

Drugs in Context is published by BioExcel Publishing Ltd. Registered office: 6 Green Lane Business Park, 238 Green Lane, New Eltham, London, SE9 3TL, UK.

BioExcel Publishing Limited is registered in England Number 10038393. VAT GB 252 7720 07.

For all manuscript and submissions enquiries, contact the Editorial office editorial@drugsincontext.com

For all permissions, rights and reprints, contact David Hughes david.hughes@bioexcelpublishing.com

## References

- 1. Wat D. The common cold: a review of the literature. Eur J Intern Med. 2004;15(2):79-88. https://doi.org/10.1016/j.ejim.2004.01.006
- 2. Heikkinen T, Järvinen A. The common cold. Lancet. 2003;361(9351):51–59. https://doi.org/10.1016/S0140-6736(03)12162-9
- 3. Eccles R. Is the common cold a clinical entity or a cultural concept? *Rhinology*. 2013;51(1):3–8. https://doi.org/10.4193/Rhino12.123
- 4. Jin X, Ren J, Li R, et al. Global burden of upper respiratory infections in 204 countries and territories, from 1990 to 2019. *EClinicalMedicine*. 2021;37:100986. https://doi.org/10.1016/j.eclinm.2021.100986
- Jackson GG, Dowling HF, Spiesman IG, Boand AV. Transmission of the common cold to volunteers under controlled conditions. I. The common cold as a clinical entity. *AMA Arch Intern Med*. 1958;101(2):267–278. https://doi.org/10.1001/archinte.1958.00260140099015
- 6. Lev E. Ethno-diversity within current ethno-pharmacology as part of Israeli traditional medicine a review. *J Ethnobiol Ethnomed*. 2006;2:4. https://doi.org/10.1186/1746-4269-2-4
- 7. Ibarra-Coronado EG, Pantaleón-Martínez AM, Velázquez-Moctezuma J, et al. The bidirectional relationship between sleep and immunity against infections. *J Immunol Res*. 2015;2015:678164. https://doi.org/10.1155/2015/678164
- 8. Wilder-Smith A, Mustafa FB, Earnest A, Gen L, Macary PA. Impact of partial sleep deprivation on immune markers. *Sleep Med*. 2013;14(10):1031–1034. https://doi.org/10.1016/j.sleep.2013.07.001
- 9. Wentz LM, Ward MD, Potter C, et al. Increased risk of upper respiratory infection in military recruits who report sleeping less than 6 h per night. *Mil Med*. 2018;183(11–12):e699–e704. https://doi.org/10.1093/milmed/usy090
- 10. Centers for Disease Control and Prevention. Common Cold. https://www.cdc.gov/antibiotic-use/colds.html. Accessed 16 May 2022.
- 11. Eccles R. Understanding the symptoms of the common cold and influenza. *Lancet Infect Dis.* 2005;5(11):718–725. https://doi.org/10.1016/S1473-3099(05)70270-X
- 12. Witek TJ, Ramsey DL, Carr AN, Riker DK. The natural history of community-acquired common colds symptoms assessed over 4-years. *Rhinology*. 2015;53(1):81–88. https://doi.org/10.4193/Rhino14.149
- 13. Turner RB. Epidemiology, pathogenesis, and treatment of the common cold. *Ann Allergy Asthma Immunol*. 1997;78(6):531–539; quiz 539–540. https://doi.org/10.1016/S1081-1206(10)63213-9
- 14. Hendley JO. The host response, not the virus, causes the symptoms of the common cold. *Clin Infect Dis.* 1998;26(4):847–848. https://doi.org/10.1086/513921
- 15. Eccles R. Pathophysiology of nasal symptoms. Am J Rhinol. 2000;14(5):335-338. https://doi.org/10.2500/105065800781329528
- 16. Conti B, Tabarean I, Andrei C, Bartfai T. Cytokines and fever. Front Biosci. 2004;9:1433–1449. https://doi.org/10.2741/1341
- 17. Proud D, Reynolds CJ, Lacapra S, Kagey-Sobotka A, Lichtenstein LM, Naclerio RM. Nasal provocation with bradykinin induces symptoms of rhinitis and a sore throat. *Am Rev Respir Dis.* 1988;137(3):613–616. https://doi.org/10.1164/ajrccm/137.3.613
- Shibayama Y, Skoner D, Suehiro S, Konishi JE, Fireman P, Kaplan AP. Bradykinin levels during experimental nasal infection with rhinovirus and attenuated influenza virus. *Immunopharmacology*. 1996;33(1–3):311–313. https://doi.org/10.1016/0162-3109(96)00051-3
- 19. Eccles R. Mechanisms of symptoms of common cold and flu. In Eccles R, Weber D, eds. *Common Cold*. Birkhäuser Verlag; 2009:23–45. https://doi.org/10.1007/978-3-7643-9912-2\_2
- 20. Beutler B. Science review: key inflammatory and stress pathways in critical illness the central role of the Toll-like receptors. *Crit Care*. 2003;7(1):39–46. https://doi.org/10.1186/cc1828
- 21. Exton MS. Infection-induced anorexia: active host defence strategy. *Appetite*. 1997;29(3):369–383. https://doi.org/10.1006/appe.1997.0116
- 22. Georgitis JW. Nasopharyngitis, pharyngitis, and tonsillitis. *Immunol Allergy Clin North Am*. 1993;13:109–118. https://doi.org/10.1016/S0889-8561(22)00434-9
- 23. Eccles R. Efficacy and safety of over-the-counter analgesics in the treatment of common cold and flu. *J Clin Pharm Ther.* 2006;31(4):309–319. https://doi.org/10.1111/j.1365-2710.2006.00754.x

- 24. Eccles R, Loose I, Jawad M, Nyman L. Effects of acetylsalicylic acid on sore throat pain and other pain symptoms associated with acute upper respiratory tract infection. *Pain Med*. 2003;4(2):118–124. https://doi.org/10.1046/j.1526-4637.2003.03019.x
- 25. Mygind N, Secher C, Kirkegaard J. Role of histamine and antihistamines in the nose. 1983;128(Pt 1):16–20.
- 26. Eccles R. Physiology of nasal secretion. Eur J Respir Dis. 1983;62:115–119.
- 27. Davis SS, Eccles R. Nasal congestion: mechanisms, measurement and medications. Core information for the clinician. *Clin Otolaryngol Allied Sci*. 2004;29(6):659–666. https://doi.org/10.1111/j.1365-2273.2004.00885.x
- 28. Malcomson KG. The vasomotor activities of the nasal mucous membrane. *J Laryngol Otol*. 1959;73(2):73–98. https://doi.org/10.1017/s0022215100054980
- 29. Eccles R. Sympathetic control of nasal erectile tissue. Eur J Respir Dis Suppl. 1983;128(Pt 1):150–154.
- 30. Lacroix JS, Stjärne P, Anggärd A, Lundberg JM. Sympathetic vascular control of the pig nasal mucosa (III): co-release of noradrenaline and neuropeptide Y. *Acta Physiol Scand*. 1989;135(1):17–28. https://doi.org/10.1111/j.1748-1716.1989.tb08546.x
- 31. Eccles R, Eriksson M, Garreffa S, Chen SC. The nasal decongestant effect of xylometazoline in the common cold. *Am J Rhinol*. 2008;22(5):491–496. https://doi.org/10.2500/ajr.2008.22.3202
- 32. Bickford L, Shakib S, Taverner D. The nasal airways response in normal subjects to oxymetazoline spray: randomized doubleblind placebo-controlled trial. *Br J Clin Pharmacol.* 1999;48(1):53–56. https://doi.org/10.1046/j.1365-2125.1999.00972.x
- 33. Eccles R, Jawad MS, Jawad SS, Angello JT, Druce HM. Efficacy and safety of single and multiple doses of pseudoephedrine in the treatment of nasal congestion associated with common cold. *Am J Rhinol*. 2005;19(1):25–31.
- 34. Clarke JD, Eccles R. Paradoxical sensation of nasal airflow in patients with common cold. Are we measuring the correct modality? *Acta Otolaryngol.* 2005;125(12):1307–1311. https://doi.org/10.1080/00016480510043404
- 35. Falck B, Svanholm H, Aust R, Bäcklund L. The relationship between body posture and pressure in occluded maxillary sinus of man. *Rhinology*. 1989;27(3):161–167.
- 36. Falck B, Svanholm H, Aust R, Bäcklund L. Blood flow and pulse amplitude in the mucosa of the human maxillary sinus in relation to body posture. *Rhinology*. 1990;28(3):169–176.
- 37. Lee PC, Cotterill-Jones C, Eccles R. Voluntary control of cough. *Pulm Pharmacol Ther*. 2002;15(3):317–320. https://doi.org/10.1006/pupt.2002.0365
- 38. Widdicombe J, Eccles R, Fontana G. Supramedullary influences on cough. *Respir Physiol Neurobiol*. 2006;152(3):320–328. https://doi.org/10.1016/j.resp.2006.02.018
- 39. Simonyan K, Saad ZS, Loucks TM, Poletto CJ, Ludlow CL. Functional neuroanatomy of human voluntary cough and sniff production. *Neuroimage*. 2007;37(2):401–409. https://doi.org/10.1016/j.neuroimage.2007.05.021
- 40. Eccles R, Lee PC. Cough induced by airway vibration as a model of airway hyperreactivity in patients with acute upper respiratory tract infection. *Pulm Pharmacol Ther*. 2004;17(6):337–342. https://doi.org/10.1016/j.pupt.2004.09.011
- 41. Jacoby DB. Pathophysiology of airway viral infections. *Pulm Pharmacol Ther*. 2004;17(6):333–336. https://doi.org/10.1016/j.pupt.2004.09.014
- 42. Leon LR. Invited review: cytokine regulation of fever: studies using gene knockout mice. *J Appl Physiol*. 2002;92(6): 2648–2655. https://doi.org/10.1152/japplphysiol.01005.2001
- 43. Netea MG, Kullberg BJ, Van der Meer JW. Circulating cytokines as mediators of fever. *Clin Infect Dis*. 2000;31(Suppl. 5):S178–S184. https://doi.org/10.1086/317513
- 44. Baracos V, Rodemann HP, Dinarello CA, Goldberg AL. Stimulation of muscle protein degradation and prostaglandin E2 release by leukocytic pyrogen (interleukin-1). A mechanism for the increased degradation of muscle proteins during fever. *N Engl J Med*. 1983;308(10):553–558. https://doi.org/10.1056/NEJM198303103081002
- 45. Kotler DP. Cachexia. Ann Intern Med. 2000;133(8):622–634. https://doi.org/10.7326/0003-4819-133-8-200010170-00015
- 46. Smith AP. Sleep and the common cold. J Behav Health. 2012;1:114–117.
- 47. Meltzer EO. Does rhinitis compromise night-time sleep and daytime productivity? Clin Exp All Rev. 2002;2:67–72.
- 48. Dicpinigaitis PV, Colice GL, Goolsby MJ, Rogg Gl, Spector SL, Winther B. Acute cough: a diagnostic and therapeutic challenge. *Cough*. 2009;5:11. https://doi.org/10.1186/1745-9974-5-11
- 49. Sabharwal G, Craig TJ. The effect of rhinitis on sleep, quality of life, daytime somnolence, and fatigue. In Mahmoudi M, ed. *Allergy and Asthma*. Springer International Publishing; 2016:87–97. https://doi.org/10.1007/978-3-319-30835-7\_7
- 50. Drake CL, Roehrs TA, Royer H, Koshorek G, Turner RB, Roth T. Effects of an experimentally induced rhinovirus cold on sleep, performance, and daytime alertness. *Physiol Behav*. 2000;71(1–2):75–81. https://doi.org/10.1016/s0031-9384(00)00322-x
- 51. Morice AH, Marshall AE, Higgins KS, Grattan TJ. Effect of inhaled menthol on citric acid induced cough in normal subjects. *Thorax*. 1994;49(10):1024–1026. https://doi.org/10.1136/thx.49.10.1024
- 52. Jessen M, Malm L. The importance of nasal airway resistance and nasal symptoms in the selection of patients for septoplasty. *Rhinology*. 1984;22(3):157–164.
- 53. Hensel H, Zotterman Y. The effect of menthol on the thermoreceptors. *Acta Physiol Scand*. 1951;24(1):27–34. https://doi.org/10.1111/j.1748-1716.1951.tb00824.x

- 54. McBride B, Whitelaw WA. A physiological stimulus to upper airway receptors in humans. *J Appl Physiol Respir Environ Exerc Physiol*. 1981;51(5):1189–1197. https://doi.org/10.1152/jappl.1981.51.5.1189
- 55. White DP, Cadieux RJ, Lombard RM, Bixler EO, Kales A, Zwillich CW. The effects of nasal anesthesia on breathing during sleep. *Am Rev Respir Dis.* 1985;132(5):972–975. https://doi.org/10.1164/arrd.1985.132.5.972
- 56. Eccles R, Lancashire B, Tolley NS. Experimental studies on nasal sensation of airflow. *Acta Otolaryngol*. 1987;103(5–6):303–306. https://doi.org/10.3109/00016488709107798
- 57. Santhi N, Ramsey D, Phillipson G, Hull D, Revell VL, Dijk D-J. Efficacy of a topical aromatic rub (Vicks VapoRub<sup>†</sup>) on effects on self-reported and actigraphically assessed aspects of sleep in common cold patients. *Open J Resp Dis*. 2017;7:83–101. https://doi.org/10.4236/ojrd.2017.72009
- 58. Omar S, Clarke R, Abdullah H, et al. Respiratory virus infection up-regulates TRPV1, TRPA1 and ASICS3 receptors on airway cells. *PLoS ONE*. 2017;12(2):e0171681. https://doi.org/10.1371/journal.pone.0171681
- Abdullah H, Heaney LG, Cosby SL, McGarvey LP. Rhinovirus upregulates transient receptor potential channels in a human neuronal cell line: implications for respiratory virus-induced cough reflex sensitivity. *Thorax*. 2014;69(1):46–54. https://doi.org/10.1136/thoraxjnl-2013-203894
- 60. McKemy DD, Neuhausser WM, Julius D. Identification of a cold receptor reveals a general role for TRP channels in thermosensation. *Nature*. 2002;416(6876):52–58. https://doi.org/10.1038/nature719
- 61. Bautista DM, Siemens J, Glazer JM, et al. The menthol receptor TRPM8 is the principal detector of environmental cold. *Nature*. 2007;448(7150):204–208. https://doi.org/10.1038/nature05910
- 62. Eccles R, Jawad M, Ramsey DL, Hull JC. Efficacy of a topical aromatic rub (Vicks VapoRub<sup>†</sup>)-speed of action of subjective nasal cooling and relief from nasal congestion. *Open J Respir Dis*. 2015;5:10–18. https://doi.org/10.4236/ojrd.2015.51002
- 63. Xu H, Blair NT, Clapham DE. Camphor activates and strongly desensitizes the transient receptor potential vanilloid subtype 1 channel in a vanilloid-independent mechanism. *J Neurosci*. 2005;25(39):8924–8937. https://doi.org/10.1523/JNEUROSCI.2574-05.2005
- 64. Juergens UR. Anti-inflammatory properties of the monoterpene 1.8-cineole: current evidence for co-medication in inflammatory airway diseases. *Drug Res (Stuttg)*. 2014;64(12):638–646. https://doi.org/10.1055/s-0034-1372609
- 65. Caceres AI, Liu B, Jabba SV, Achanta S, Morris JB, Jordt SE. Transient receptor potential cation channel subfamily M member 8 channels mediate the anti-inflammatory effects of eucalyptol. *Br J Pharmacol*. 2017;174(9):867–879. https://doi.org/10.1111/bph.13760
- 66. Burrow A, Eccles R, Jones AS. The effects of camphor, eucalyptus and menthol vapour on nasal resistance to airflow and nasal sensation. *Acta Otolaryngol*. 1983;96(1–2):157–161. https://doi.org/10.3109/00016488309132886
- 67. Pereira EJ, Sim L, Driver H, Parker C, Fitzpatrick M. The effect of inhaled menthol on upper airway resistance in humans: a randomized controlled crossover study. *Can Respir J*. 2013;20(1):e1–e4. https://doi.org/10.1155/2013/383019
- 68. Packman EW, London SJ. The utility of artificially induced cough as a clinical model for evaluating the antitussive effects of aromatics delivered by inunction. *Eur J Respir Dis Suppl*. 1980;110:101–109.
- 69. Ben-Arye E, Dudai N, Eini A, Torem M, Schiff E, Rakover Y. Treatment of upper respiratory tract infections in primary care: a randomized study using aromatic herbs. *Evid Based Complement Alternat Med*. 2011;2011:690346. https://doi.org/10.1155/2011/690346
- 70. Kamin W, Kieser M. Pinimenthol<sup>‡</sup> ointment in patients suffering from upper respiratory tract infections a post-marketing observational study. *Phytomedicine*. 2007;14(12):787–791. https://doi.org/10.1016/j.phymed.2007.09.024
- 71. Paul IM, Beiler JS, King TS, Clapp ER, Vallati J, Berlin CM Jr. Vapor rub, petrolatum, and no treatment for children with nocturnal cough and cold symptoms. *Pediatrics*. 2010;126(6):1092–1099. https://doi.org/10.1542/peds.2010-1601

<sup>&</sup>lt;sup>+</sup>Vicks vaporub is a registered product, marketed globally and manufactured by Proctor & Gamble. Headquarters: Cincinnati, Ohio, United States of America

<sup>&</sup>lt;sup>‡</sup> Pinimenthol is a registered product manufactured by Dr Willmar Schwabe GmbH & Co. KG. Headquarters: Karlsruhe, Baden-Württemberg, Germany