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## Essential oils as complementary and alternative medicines for the treatment of influenza

**William N Setzer**

### Abstract

Influenza is a common infectious respiratory disease that not only causes seasonal outbreaks, but can also cause deadly global pandemics. Herbal medicines have been used for centuries to treat symptoms of influenza and essential oils derived from them have been prescribed as complementary and alternative treatments against influenza. This review presents a summary of essential oils that have shown anti-influenza activity, the typical compositions of the oils, as well as essential oil components that have shown anti-influenza activity

**Keywords:** Influenza, essential oils, antiviral

### 1. Introduction

#### 1.1 Influenza – What is “the flu”?

Influenza is an infectious respiratory disease caused by one of three types of influenza viruses, Type A, Type B, and Type C [1]. Influenza virus type A is the most significant in terms of human morbidity and mortality. This species is found in a wide variety of bird and mammal species [2], and several different serotypes have caused global flu pandemics [3]: H1N1, which caused the Spanish Flu in 1918 (40-50 million deaths worldwide) [4] and the Swine Flu in 2009 [5]; H2N2, which caused the Asian Flu in 1957 (> 1 million deaths worldwide) [5]; H3N2, which caused the Hong Kong Flu in 1968 [6]; and H5N1, which caused the Bird Flu in 2004 [7]. Influenza virus type B is largely confined to human hosts [8]. This virus species mutates around 2-3 times slower than type A, so there is some degree of immunity to re-infection [9]. Influenza virus type C is less common than types A and B, and the effects are generally mild [10].

The Centers for Disease Control and Prevention (CDC) recommends annual flu vaccine for everyone 6 months and older. Nevertheless, because the virus, especially type A, mutates readily and there are several serovars in circulation in the human population as well as mammal and avian hosts, the chances of influenza infection are not zero. Current antiviral agents for influenza include amantadine, rimantadine, oseltamivir (Tamiflu®), and zanamivir (Relenza®) [11]. These agents have been approved by the FDA for prophylaxis as well as treatment for influenza A infections; oseltamivir and zanamivir are also active against influenza B.

### 2. Essential Oils and Influenza Virus

Essential oils have been reported to be complementary and alternative treatment options for influenza infections [12], and several essential oils and essential oil components have shown anti-influenza virus activity. In addition, essential oils and their components can also serve to treat symptoms of influenza.

#### 2.1 Bergamot Oil

Bergamot essential oil is generally obtained by cold pressing the rind of *Citrus bergamia* (Rutaceae) fruit [13], but can also be obtained by hydrodistillation [14]. Bergamot oil is rich in monoterpenoids, especially limonene (23-55%), linalool (2-37%), linalyl acetate (12-41%), with lesser quantities of  $\beta$ -pinene (up to 10%) and  $\gamma$ -terpinene (up to 10%) [15-19]. Vimalanathan and Hudson [20] have shown bergamot oil to demonstrate *in vitro* anti influenza virus activity (100% inhibition of type A H1N1 at a concentration of 0.3%). In addition, these workers found 95% H1N1 virus inhibition after 10 min exposure to bergamot oil vapor. In addition to anti-influenza activity, bergamot oil has also shown antimicrobial, anti-inflammatory, antiproliferative, anxiolytic, and antinociceptive properties [13].

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## 2.2 Cinnamon Leaf Oil

The leaf essential oil of *Cinnamomum zeylanicum* (Lauraceae) showed 100% *in vitro* inhibition of influenza type A (H1N1) virus at 0.3% as well as 100% inhibition of H1N1 virus after 30 min exposure to cinnamon leaf oil vapor<sup>[20]</sup>. *C. zeylanicum* leaf oil is typically dominated by eugenol (75-85%), followed by smaller amounts of linalool (1.6-8.5%), (*E*)-cinnamaldehyde (0.6-1.5%), (*E*)-cinnamyl acetate (0.7-2.6%),  $\beta$ -caryophyllene (0.5-6.7%), eugenyl acetate (0.1-2.9%), and benzyl benzoate (0.1-8.3%)<sup>[21-23]</sup>. There are, however, other chemotypes of *C. zeylanicum*, including a  $\beta$ -caryophyllene-rich (53%) chemotype<sup>[24]</sup> and a 1,8-cineole/*o*-cymene chemotype<sup>[25]</sup>.

## 2.3 Eucalyptus Oil

There are numerous species of the genus *Eucalyptus* (Myrtaceae), originally from Australia, but now cultivated worldwide. Medicinal eucalyptus oil is rich in 1,8-cineole and is derived from the leaves of *E. globulus* (blue gum), *E. polybractea* (blue mallee), and *E. kochii* (oil mallee)<sup>[26, 27]</sup>. *E. globulus* essential oil showed 90% inhibition of influenza type A (H1N1) virus at 0.3% concentration as well as 90% inhibition of the virus after 10 min exposure to the vapor<sup>[20]</sup>. The leaf oil of commercial Australian *E. globulus* is dominated by 1,8-cineole (syn. eucalyptol, 81-84%), but also containing limonene (8-12%),  $\alpha$ -pinene (2-4%), and *p*-cymene (~2%)<sup>[28]</sup>. The essential oil compositions are variable, depending on the geographical origin, with 1,8-cineole concentrations ranging from 17% to 90%<sup>[29]</sup>.

The leaf oil of *E. polybractea* showed 100% inhibition of influenza type A (H1N9) airborne virus after 30 min exposure to the essential oil vapor<sup>[30]</sup>. *E. polybractea* leaf oil is rich in 1,8-cineole (87-94%), with smaller concentrations of  $\alpha$ -pinene (up to 1.1%), sabinene (up to 1.0%),  $\beta$ -pinene (up to 2.3%), limonene (up to 1.9%), *p*-cymene (up to 2.8%), and terpinen-4-ol (up to 2.8%)<sup>[31, 32]</sup>. The high concentration of 1,8-cineole in eucalyptus oils likely contributes to its efficacy against some of the symptoms of influenza. Although 1,8-cineole has been shown not to have antitussive activity<sup>[33, 34]</sup>, the compound has shown clinical efficacy as a mucolytic and spasmolytic as well as beneficial effects in inflammatory airway diseases such as asthma and chronic obstructive pulmonary disease (COPD)<sup>[35, 36]</sup>. The compound has shown efficacy in acute rhinosinusitis and alleviates headache, nasal obstruction, and rhinological secretion in a double-blind, placebo-controlled study<sup>[37]</sup>. In addition, 1,8-cineole has demonstrated ulcer-healing and gastroprotective properties in rats<sup>[38]</sup> as well as antispasmodic effects on isolated mouse ileum<sup>[39]</sup>.

## 2.4 Geranium Oil

Geranium oil is the hydrodistilled essential oil from the aerial parts of rose-scented geranium (*Pelargonium graveolens*, Geraniaceae). *P. graveolens* is native to southern Africa, but is now cultivated worldwide. The main components of geranium oil are somewhat variable, depending on the geographical location and phenological stage, but the oils are generally dominated by citronellol (21.9-37.5%), citronellyl formate (9.8-20.6%), geraniol (6.0-16.5%), geranyl formate (1.5-6.5%), menthone (up to 13%), isomenthone (up to 9.9%), and linalool (0.8-14.9%)<sup>[40-44]</sup>. A cultivated sample of *P. graveolens* from Bosnia and Herzegovina showed 50.2% geraniol with reduced citronellol (14.2%)<sup>[45]</sup>. Geranium oil has shown 80% *in vitro* inhibition of influenza type A (H1N1) virus at 0.3% as well as 95% inhibition of H1N1 virus after 30

min exposure to the vapor<sup>[20]</sup>. Geraniol has been found not be active against influenza virus type A (H3N2)<sup>[46]</sup>.

## 2.5 Lavender Oil

Lavender essential oil is obtained by hydrodistillation of the floral spikes of *Lavandula angustifolia* (Lamiaceae). Lavender oil showed 85% *in vitro* inhibition of influenza type A (H1N1) virus at 0.3% as well as 80% inhibition of H1N1 virus after 30 min exposure to lavender oil vapor<sup>[20]</sup>. *L. angustifolia* essential oil is rich in linalyl acetate (37.0-43.6%), linalool (19.7-39.1%), geraniol (up to 9.3%),  $\beta$ -caryophyllene (up to 5.1%), terpinene-4-ol (up to 14.9%), lavandulol (up to 1.5%), lavandulyl acetate (up to 5.5%), 1,8-cineole (up to 4.1%), and borneol (up to 6.4%)<sup>[47-50]</sup>.

## 2.6 Lemon Balm Oil

Lemon balm oil, the hydrodistilled oil from the aerial parts of *Melissa officinalis* (Lamiaceae), has shown antiviral activity against avian influenza A virus (H9N2)<sup>[51]</sup>. Thus, at concentrations as low as 5 ppm, *M. officinalis* essential oil showed remarkable *in vitro* viral infection reduction. Lemon balm oil is dominated by the citrals, neral and geraniol. Neral concentrations generally range 17-32% and geraniol concentrations are usually higher (23-43%), with some geraniol concentrations as high as 85%. Other components in lemon balm oil include linalool (up to 9.0%), citronellal (0.7-20.3%), geraniol (up to 23.2%),  $\beta$ -caryophyllene (up to 11.3%), and caryophyllene oxide (0.4-31.7%)<sup>[51-56]</sup>. Citral (mixture of neral and geraniol), linalool, and geraniol have shown antiviral activity against human parainfluenza virus type 3, but citronellal was inactive<sup>[57]</sup>.

## 2.7 Lemongrass Oil

Lemongrass (*Cymbopogon flexuosus*, Poaceae) essential oil has shown 100% inhibition of influenza virus type A (H1N1) at an essential oil concentration of 0.3% as well as 90% inhibition after 30 min exposure to lemongrass oil vapor<sup>[20]</sup>. Geraniol (48-54%) and neral (29-33%), have been reported as the major components of *C. flexuosus*<sup>[58, 59]</sup>, but many chemotypes, cultivars, and variants have been reported for *C. flexuosus*<sup>[60-69]</sup>. Geraniol and neral are likely responsible for the antiviral activity of lemongrass oil (see above).

## 2.8 Tea Tree Oil

Tea tree oil is the hydrodistilled essential oil from the leaves of *Melaleuca alternifolia* (Myrtaceae). Six different chemotypes of tea tree oil have been identified, correlating somewhat with geographical location of natural populations in Australia<sup>[70]</sup>. These chemotypes include a terpinen-4-ol chemotype, a 1,8-cineole chemotype, a terpinolene chemotype, and three mixed chemotypes, 1,8-cineole/terpinen-4-ol, 1,8-cineole/terpinolene, and 1,8-cineole/terpinolene/terpinen-4-ol. Commercial tea tree oil is composed of terpinen-4-ol (30-48%),  $\gamma$ -terpinene (10-28%),  $\alpha$ -terpinene (5-13%), 1,8-cineole (up to 15%), terpinolene (1.5-5%), *p*-cymene (0.5-12%),  $\alpha$ -pinene (1-6%), and  $\alpha$ -terpineol (1.5-8%)<sup>[71]</sup>. Tea tree oil showed 100% inhibition of influenza type A (H1N1) virus at 0.01% concentration and a median inhibitory concentration (IC<sub>50</sub>) of 6 ppm<sup>[72, 73]</sup>. In addition, 30 min exposure of type A (H1N9) virus to tea tree oil vapor caused 100% inhibition<sup>[30]</sup>. The tea tree oil components, terpinen-4-ol, terpinolene, and  $\alpha$ -terpineol, have shown anti-influenza virus activity against type A (H1N1) with IC<sub>50</sub> values of 25, 12, and 250 ppm, respectively<sup>[72]</sup>.  $\alpha$ -Terpinene,  $\gamma$ -terpinene, and *p*-cymene were inactive, however.

On the other hand, terpinen-4-ol has shown antimicrobial activity against several respiratory tract pathogens, including *Haemophilus influenzae*, *Streptococcus pneumoniae* [74], *Aspergillus niger*, *A. flavus*, and *A. fumigatus* [75].

## 2.9 Thyme Oil

*Thymus vulgaris* (Lamiaceae) essential oil has shown 100% inhibition of type A (H1N1) virus at 0.3% concentration as well as 70% inhibition of the virus after 30 min exposure to the vapor [20]. The chemical composition of thyme oil has been extensively studied from collections all over the world, and there have been at least 20 different chemotypes identified [76]. The “typical” thyme oil is the thymol chemotype with an average thymol content of 45% (range 31-50%), but also with significant concentrations of *p*-cymene (0.1-26.6%, average = 15.6%) and  $\gamma$ -terpinene (up to 22.8%, average = 9.3%). In addition, there are several other chemotypes of *T. vulgaris* rich in thymol and/or carvacrol [76]. Thymol has been identified as an anti-influenza agent [77]. In addition, both thymol and carvacrol have shown antitussive activity [78, 79], while thymol has shown antiviral activity against parainfluenza type 3 virus [57].

## 2.10 “Bai Qian” Root Oil

Roots of “Bai Qian”, *Cynanchum stauntonii* (Asclepiadaceae), have been used in Chinese traditional medicine as antitussives and expectorants [80]. The volatile oil from the roots of *C. stauntonii* was obtained by hydrodistillation and screened for antiviral activity against influenza type A (H1N1) [81]. The essential oil showed *in-vitro* antiviral activity with IC<sub>50</sub> of 64 ppm. In addition, in an *in-vivo* assay using a mouse model, a dose of 300 mg/(kg day) gave a 100% survival outcome. The major components in the essential oil were (2*E*,4*E*)-decadienal (23.0%),  $\gamma$ -nonalactone (4.2%), 5-pentyl-2(3*H*)-furanone (3.8%), 3-isopropyl-1-pentanol (3.5%), caryophyllene oxide (3.1%), and (2*E*,4*Z*)-decadienal (3.0%).

## 2.11 “Yuxingcao” Root Oil

*Houttuynia cordata* (Saururaceae), also known as “Dokudami” (Japanese), “Phak Khao Thong” (Thai), or “Fishwort” (English), has been used for hundreds of years in Chinese traditional medicine to relieve flu-like respiratory difficulties such as phlegm, cough, and shortness of breath [82]. There have been several reports on the essential oil composition from the aerial parts of *H. cordata* [83-85]. The essential oil is characterized by fatty-acid-derived compounds such as decanal (3.4-8.9%), decanol (up to 7.0%), 2-undecanone (23.0-36.1%), decanoic acid (1.4-6.3%), dodecanal (up to 7.3%), and 2-tridecanone (2.6-5.6%). *H. cordata* essential oil has been screened for antiviral activity against influenza type A (H1N1) and showed activity with IC<sub>50</sub> of 48 ppm [86]. Three *H. cordata* essential oil components, 2-undecanone, dodecanal, and octanal, were also screened; IC<sub>50</sub> = 62, 51, and 15 ppm, respectively.

## 2.12 Essential Oil Components

In addition to the essential oil components noted above, several volatile compounds have shown anti-influenza activity. (*E*)-Cinnamaldehyde demonstrated *in-vitro* antiviral activity with 70% inhibition of type A (H1N1) virus at a concentration of 0.53% after 3 h [87]. The compound also showed *in-vivo* activity with as 89% inhibition of H1N1 virus after inhalation in a mouse model. (*E*)-Cinnamaldehyde is the major component (58-98%) of cinnamon (*Cinnamomum*

*zeylanicum*) bark essential oil [88-91]. Cinnamaldehyde has also shown activity against respiratory tract pathogenic fungi *Aspergillus niger*, *A. fumigatus*, *A. nidulans*, *A. flavus*, *Candida albicans*, *C. tropicalis*, *C. pseudotropicalis*, and *Histoplasma capsulatum* [92], and bacteria *Haemophilus influenzae*, *Streptococcus pneumoniae* [74]. Apparently, cinnamon bark oil itself has not been tested for anti-influenza activity.

At a concentration of 0.22%, the sesquiterpenoid ketone germacrone has shown 80-90% inhibition of influenza type A (H1N1) virus, 80% inhibition of type A (H3N2), and 75-100% inhibition of type B virus [93]. Germacrone is abundant in the aerial parts essential oil of *Baccharis salicifolia* (42%) [94], the fruit essential oil of *Eugenia uniflora* (28%) [95], the leaf essential oil of *Siparuna grandiflora* (67%) [96], and the aerial parts essential oil of *Geranium macrorrhizum* (50%) [97]. To date, none of these plants has been screened for anti-influenza activity.

Patchouli alcohol has been screened for anti-influenza activity both *in vitro* and *in vivo*. The compound showed 89% inhibition of type A (H1N1) virus at 10 ppm [98]. Against type A (H2N2), patchouli alcohol was active *in vitro* with an IC<sub>50</sub> of 0.89 ppm [99]. In an *in-vivo* test using a mouse model patchouli alcohol showed a 70% survival rate at a dose of 5 mg/(kg day) [99]. Patchouli (*Pogostemon cablin*) essential oil contains about 23-54% patchouli alcohol [100-102]. There have apparently been no studies on anti-influenza activity of patchouli oil; the methanol extract, however, did show activity against type A (H1N1) (99.8% inhibition at 10 ppm) [98].

$\beta$ -Santalol has shown 86% inhibition of type A (H3N2) influenza virus at a concentration of 0.01% [103]. Commercial sandalwood (*Santalum album*) essential oil contains 40-50%  $\beta$ -santalol along with 15-25%  $\alpha$ -santalol [104]. Sandalwood oil has apparently not been screened for anti-influenza activity.

## 3. Conclusions

Essential oils have shown promise in prevention and treatment of influenza infections, corroborating much of the traditional medicinal use of the corresponding plants. In addition to their antiviral activities, many of the essential oils can also relieve some of the symptoms of influenza. There are many opportunities for additional research on antiviral essential oils and essential oil components with respect to influenza infection, including screening of additional essential oils, isolation and screening of essential oil components, and evaluation of antiviral mechanisms of activity. Although essential oils have shown antiviral activity and may be considered as complementary and alternative treatment for influenza infection, this report is intended for information only and not recommended for self-medication. Please consult your health provider for treatment options for the flu.

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