

Review Article

Effective Antiviral Activity of Essential Oils and their Characteristic Terpenes against Coronaviruses: An Update

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Abstract

Medicinal plants and aromatic herbs are usually used today in modern phytomedicine and alternative therapy. The essential oils (EOs) and their chemical constituents are known to be active against a wide range of viruses. Oxygenated monoterpenes and sesquiterpenes present in EOs contribute to their antiviral effect. Since the new strain of coronavirus, now named SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus), is still not completely understood, it is not yet possible to find which EOs will offer the best level of protection. More is learned about this virus on an almost weekly basis, but it could still be some considerable time before a cure is found. However, it is plausible to assume that some of the EOs and related terpenes are likely to offer a measurable level of defense in the same way that they do with many other known viruses.

ABBREVIATIONS

CoV: Coronavirus ; COVID-19: Coronavirus Disease 2019 ; EO: Essential Oil; HBV: hepatitis B virus; HeLa: Human Cervical Cancer Cell Lines; HIV: Human Immune-deficiency Virus; HSV : Herpes Simplex Viruses; IBV: Infectious Bronchitis Virus ; IL-8: Interleukin 8 ; MERS: Middle East Respiratory Syndrome; MERS-CoV: Middle East Respiratory Coronavirus; MHV: Mouse Hepatitis Virus; RNA: RiboNucleic Acid; RSV: Respiratory Syncytial Virus; SARS: Severe Acute Respiratory Syndrome; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus; TCID50: Tissue Culture Infectious Dose; TRP gene: Transient Receptor Potential gene; WHO: World Health Organization.

INTRODUCTION

The 2019 new Coronavirus, now named Severe Acute Respiratory Syndrome- Coronavirus 2 (SARS-CoV-2), has produced an epidemic of Corona Virus Disease 2019 (COVID-19) that started on 31 December 2019 in China and spread to different regions and countries. On January 30, 2020, the World Health Organization (WHO) confirmed the outbreak a worldwide health emergency. People who get sick from the novel SARS-CoV-2 may have moderate clinical symptoms, such as a fever or cough, or more severe ones, such as pneumonia [1-3].

The WHO held an update conference at their headquarters in Geneva (Switzerland) on February 11, 2020 to inform the public and people on the current extent of SARS-CoV-2, which they have now recognized as 'people enemy number one'. At the conference it was proclaimed that there have now been over 65,000 human

cases described around the globe, causing the deaths of more than 1,900 people, almost solely in China. This novel specie of Cioronavirus has not formerly been identified or known in people prior to the epidemic described in the region of Wuhan (China) last year (December 2019) [4,5] (Figure 1).

More recently (February 26, 2020), more than 2,700 people in China have died from COVID-19, as well as 52 people in other countries. Medical establishments will check any mortality in other regions or countries. Outdoor of the lockdown within China, coronavirus disease-19 cases are speeding up across the planet. The SARS-CoV-2 has really hopped the protection line. Currently, it's a real pandemic, with countries all over the globe (Figure 2), recording massive percent growth in the cases of infected human [5].

At present, we know it has got an epidemic status in South Korea and Japan. But overnight, novel human cases have been confirmed by the Iran, US, UAE, Italy, USA, Lebanon, Egypt and Algeria, among others [6,7].

WHAT IS CORONAVIRUS?

Coronaviruses (CoV), members of the Coronaviridae family, are enveloped viruses that contain non-segmented, positive-stranded genomic RNA (RiboNucleic Acid) [8,9]. Coronaviruses are a great family of viruses found in both humans and animals. Coronaviruses are single-stranded positive-sense RNA viruses that possess large viral RNA genomes [5]. Although SARS-CoV-2 is categorized in the beta-Coronaviruses group, it is different from Middle East Respiratory Syndrome Coronavirus (MERS-



Figure 1 Coronavirus spread. Flights from deadly epicenter of Virus, Wuhan, could help by reach other countries.

(Source: The U.S. Sun, updated: 22 January 2020, 12:51 GMT)

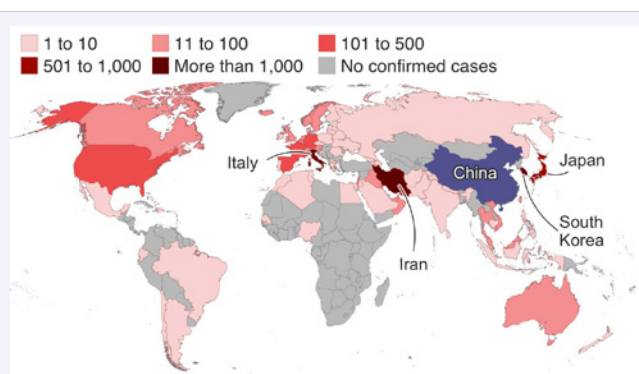


Figure 2 Cases of Coronavirus outside China.

(Source: WHO, updated: 04 March 2020, 16:00 GMT).

CoV) and SARS-CoV. Previous investigations emphasized that SARS-CoV-2 genes share <80% nucleotide identity and 89.10% nucleotide similarity with SARS-CoV genes [9,10].

The analysis of CoV ultrastructure has shown that they form pleomorphic particles that are incompletely spherical but display variations in shape and size (80–120nm in diameter). The whole SARS-CoV replication cycle take places in the cytoplasm. Overall, enveloped viruses are capable to use a diversity of cellular membranes at several steps of the virus life cycles [11-13].

Coronaviruses causes numerous illnesses comprising gastroenteritis, bronchitis and hepatitis systemic diseases on animal and humans. Both viral factors and host affect the illness severity in animals and the Coronavirus virulence. The sickness is usually most severe in babies [14,15].

Some infected people and are known to cause complaint, ranging from the common cold and fever to more severe illnesses such as Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS). Further, this Coronavirus is

not the same as SARS, but it is from the similar family of viruses. Identification of the SARS coronavirus (SARS-CoV) as the cause of SARS in the spring of 2003 stimulated research in this field [16].

HOW CORONAVIRUS SPREADS

Scientists and researchers are now investigating the new SARS-CoV to study more about how it contaminates persons. This SARS-CoV is a respiratory virus that extents mainly through direct contact with an infected human through respiratory droplets generated when they sneeze or cough, or through discharge from the nose or droplets of saliva. This is why it is extremely significant that every human should have good body hygiene. For example, the covering the nose and mouth when sneezing and coughing avoid the spread of viruses and microorganisms. Also, it is very imperative for people to wash and rinse their hands frequently with either soap and water or alcohol-based hand rub [17,18].

As of this writing, researchers report that most germs and viruses do not stay active for very long on surfaces. The COVID-19 is most probably diffused and transmitted by droplets from an infected person’s cough or sneeze, but more data are developing everyday (Figure 3).

Understandably, the possibility of a pandemic is enough to cause serious panic. While avoiding exposure to anyone likely affected is an obvious precaution, there are practical ways you can protect yourself and allay your worries.

According to the Consumer Health Information Centre (U.K), air travel and public transport give the best atmosphere for this SARS-CoV to spread. An airless atmosphere can cause human mucous membranes to become dry, which depresses the human protection against flu and colds, as does abrupt changes in body fever which reduce the body’s immunity [19,20].

We also recognize that Coronaviruses are also spread by contact, transmitted through not only evident ways, such as osculating, but by sharing drink or food utensils, telephones, pens and pencils, computer mice and keyboards, door handles and taxi. Coronaviruses can survive on hands for some hours, so at times like this common hygiene suits extremely imperative. The eyes are similarly as receptive to invading viruses as is the nose. Therefore, people should constantly wash their hands before touching their eyes, nose or mouth. Also, used materials and tissues should be disposed of closely and kitchen benches,

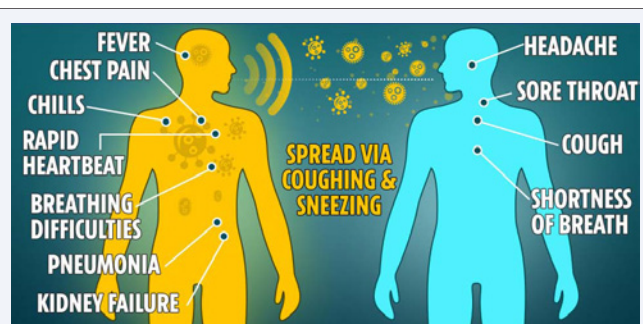


Figure 3 The symptoms of 2019-nCoV and how it spreads.

(Source: The U.S. Sun, Updated: 25 February 2020, 14:29).

bathroom units and table surfaces must be kept carefully clean [21].

Currently, there is no vaccine for the new SARS-CoV-2. Scholars and researchers have already begun investigating on one, but creating and developing a vaccine that is active and nontoxic in human beings will take a long time.

Interventionary studies involving animals or humans, and other studies require ethical approval must list the authority that provided approval and the corresponding ethical approval code.

ANTIVIRAL ACTIVITIES OF ESSENTIAL OILS AND ISOLATED COMPOUNDS

Nowadays, there are about 37 licensed antiviral drugs on the market [22], but numerous illnesses produced by viruses are not curable; latency, viral resistance, and several frequent problems in treatment are also of concern [23].

The use of EOs in aromatherapy and phytomedicine is mostly due to their antiviral antibacterial, antifungal and antioxidant effects which also is mirrored in the number of research articles published when the words “antiviral” (99,600 papers), “antibacterial” (746,000 articles), “antifungal” (160,000 articles), “anti-Coronaviruses” (11,800 papers), were used as searching criterion in google scholar website.

The exploration and search for new and promising antiviral molecules or drugs should therefore be increased and all potential approaches should be organized and deployed [24,25]. New bio-active molecules can be screened to find novel antiviral agents, as is generally carried out for cancer drug discovery.

Over 70% of the post genomically created medications and drugs have a natural origin or were motivated by natural product chemistry. Natural products and medicinal plants have usually delivered 25% to 40% of the present antibacterial, antifungal, antiviral or anticancer molecules for the pharmaceutical industry, but science has studied only a minor fraction of potentially useful herbs and plants in its efforts to design more bio-active molecules extracted from natural products [26].

The pharmaceutical industry is increasingly targeting medicinal plants with the aim of identifying lead compounds, focusing particularly on suitable alternative antiviral agents.

In recent years there has been a growing attention in the use of medicinal plants and natural substances, and some queries regarding the security of synthetic molecules have motivated more detailed and comprehensive investigations of natural products and medicinal plants [27].

Aromatic herbs and medicinal plants produce a diversity of secondary metabolites and chemical compounds with the potential to inhibit viral replication and chemical molecules from natural products are of interest as possible and promising sources to inhibit viral replication and infection. These herbs and plants have usually been used to treat a range of non-infectious and infectious illnesses and are considered as a rich source of innovative bioactive secondary metabolites [28,29]. Thus herbs and medicinal plants continue to be a main source of new lead bio-active molecules. Besides minor compounds from medicinal chemistry, medicinal plants are still key sources of inventive

beneficial agents for different diseases, comprising human infections [30].

For example, flavonoids, terpenes, polysaccharides, alkaloids, amino acids, phenols and essential oils (EOs) are among the plant-derived antiviral molecules that are being employed in phytomedicine, and these have been shown to prevent the replication of some viruses such as hepatitis B, human immunodeficiency virus, herpes simplex and SARS [24,26,31,32].

EOs, volatile and odors products extracted from medicinal plants and aromatic herbs have extensive use and application in phytomedicine and aromatherapy as well as in pharmaceutical industries. EOs are complex natural mixtures of aromatic secondary metabolites, extracted from herbs and plants using different techniques (hydro- or steam-distillation, microwave or ultrasound extractions, cold pressing or solvent extraction) [33]. The major phytochemical compounds of EOs, for example, oxygenated sesquiterpenes, monoterpenes and phenylpropanoids (Figure 4), including alcohols, aldehydes, carbohydrates, ethers and ketones, are responsible for the fragrance and pharmacological activities of medicinal plants and aromatic herbs. Different EOs and their characteristic compounds have several biological properties such as antibacterial, antifungal, antiviral, antioxidant, anti-inflammatory, wound-healing and anti-cancer effects *in vitro* and *in vivo* [34-36].

For many decades, results on the antiviral activities of EOs and their major chemical compounds lagged behind those for other germs and strains with respect to the range of EOs and viruses tested and description of the mechanisms of antiviral effect. This was revealed in the moderate few research articles and scientific publications covering the subject [37-39].

More recently, several investigations and reports have analyzed and described the *in vitro* activity of an extensive variety of EOs. The *in vitro* works have been done using the enveloped influenza or herpes simplex viruses 1 or 2 (HSV-1 or -2) [40,41].

EOs from *Origanum acutidens* [42], *Artemisia glabella* [43], *Houttuynia cordata* [44], *Salvia sclarea*, *Cynanchum stauntonii* [45], *Oenanthe crocata* [46], and *Salvia limbata* and [47], and the component cinnamaldehyde [48], have been assessed against influenza viruses.

EOs from anise (*Illicium verum*), eucalyptus and tea tree [49], hyssop (*Hyssopus officinalis*), chamomile (*Matricaria recutita*), ginger (*Zingiber officinale*), and sandalwood (*S. album*) [50], *A. aborescens* [51,52], *H. cordata* [48], *L. scoparium* [53], thyme (*Thymus vulgaris*), *Melaleuca ericifolia*, *M. leucadendron* and *M. armillaris* [54], *Salvia fruticosa* [55], *Melissa officinalis* [56,57], *M. piperita* [58], *O. crocata* [46], *S. limbata* and *S. sclarea* [47], *Santolina insularis* [60,61], *Artemisia* and *Lippia* spp. [62,63], and the components eugenol [64,65], and isoborneol [66], have been described against HSV-1 and/or -2.

Minami et al. [67], tested oils from *Juniperus communis* (juniper), *Eucalyptus globulus* (eucalyptus), *Cupressus sempervirens* (cypress), *Ocimum basilicum* album (tropical basil), *M. piperita* (peppermint), *M. alternifolia* (tea tree), *Citrus limonum* (lemon), *Cymbopogon citrates* (lemongrass), *Origanum majorana* (marjoram), *Ravensara aromatica* (ravensara), *Lavandula latifolia* (lavender), and *Rosmarinus officinalis* (rosemary) were evaluated against HSV-1.

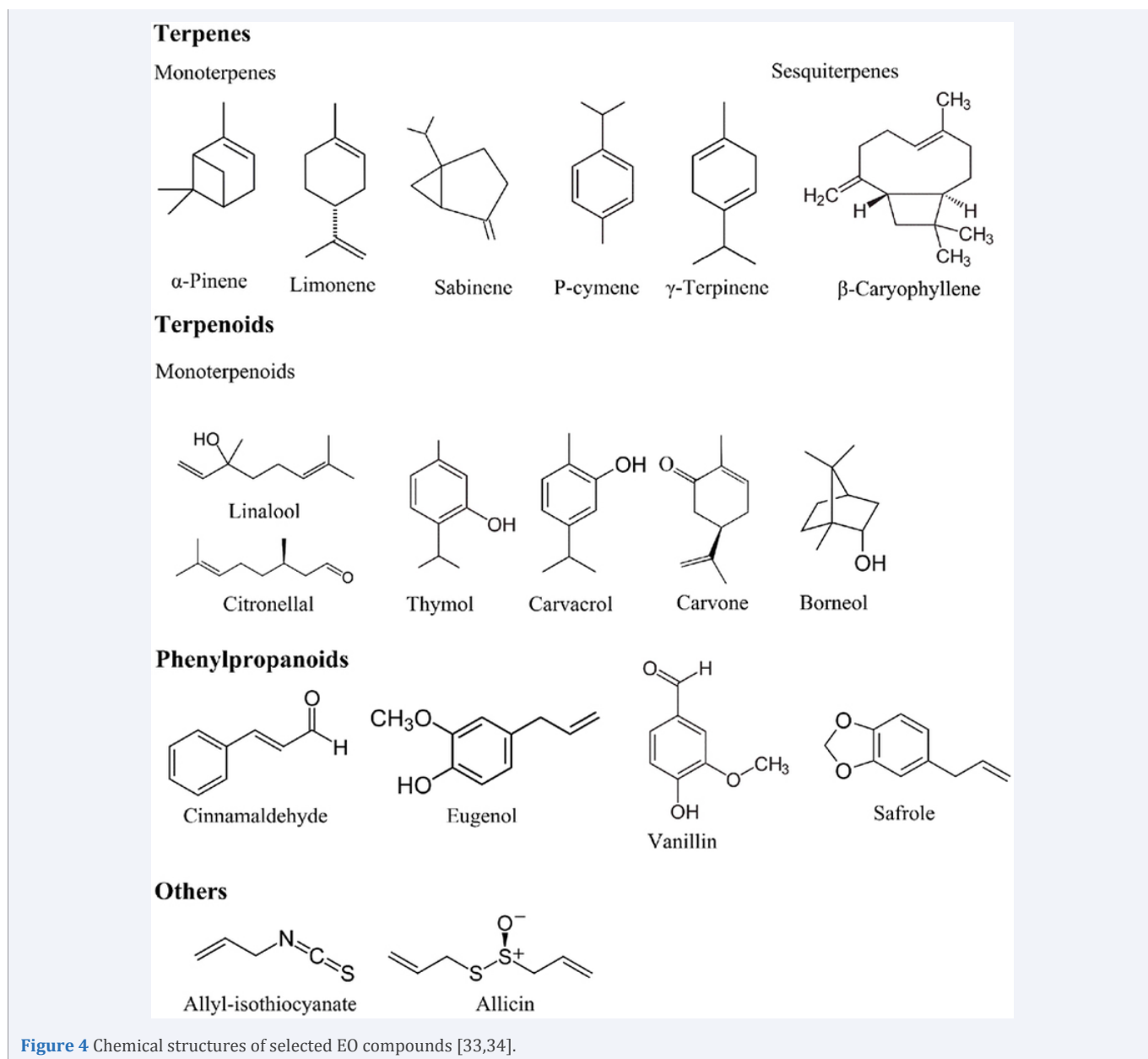


Figure 4 Chemical structures of selected EO compounds [33,34].

Most of these EOs have been tested by measuring and calculating the inhibition of plaque formation in tissue cultures of appropriate host cells *in vitro*. Overall, the doses of EOs or major constituents that decreased plaque formation by 50% ranged from 0.000 06 to 1%. Often the doses of EOs that inhibit plaque formation are only slightly lower than the quantities that prove cytotoxic to the tissue-culture cells, resulting in a moderately low therapeutic index. However, attention on the potential application of EOs as antiviral drugs still persists, principally for topical use such as skin and hand antiseptics.

Apart from the more extensively evaluated influenza virus and HSV, adenovirus and mumps virus [68], dengue virus type 2 and Junin virus [62,63], human respiratory syncytial virus [69], poliovirus [46], Human Immune-deficiency Virus (HIV) [70], Newcastle disease virus [43], tobacco mosaic virus [71], yellow fever virus [72], and the viral agent of SARS, a novel Coronavirus

[73], have also been evaluated and determined against a range of EOs and chemical compounds.

Otherwise, a chemical constituent of EOs that have an antiviral activity work like a disinfectant, and do not need replication to inhibit the virus [53,58]. Thus, resistance to virucidal compounds due to mutations generated in the viral genome during replication is unlikely [50]. The antiviral effect of EOs from botanicals has been published for a number of viruses, including dengue virus, herpes simplex virus, and Junin virus [50, 63, 74].

ANTIVIRAL ACTIVITY OF ESSENTIAL OILS AGAINST CORONAVIRUSES

Antiviral effect of a mixture of EOs and oleoresins from medicinal plants and aromatic herbs was evaluated *in vivo* and *in vitro* against Coronavirus infectious bronchitis virus [75].

Treatment of avian Infectious Bronchitis Virus (IBV), with the mixture decreased the virus titer in two host systems, Vero E6 cells and embryonating eggs. The effect of the mixture on IBV in chickens was also studied and revealed that the administration of EOs to chickens at a 1:20 dilution by spray, 2h before challenge with IBV was the most active cure. Also, current treatment reduced the severity of clinical lesions and signs in the birds, and decreased the quantity of viral RNA in the trachea. This study also revealed that the treatment with EOs protected chickens for up to 4 days post-treatment from clinical signs of disease (but not from infection) and decreased transmission of IBV over a 14-day period. Anti-IBV activity of the mixture was greater prior to virus attachment and entry indicating that the effect is virucidal. The effect appears to be more marked on cell free virus demonstrating that the effect is probably virucidal, which is significant because it may also be actual against other enveloped respiratory viruses, as well as other Coronaviruses in humans.

In the study conducted by Wen et al. [76], 221 phytochemical compounds and EOs constituents were tested for antiviral effect against severe acute respiratory syndrome associated coronavirus (SARS-CoV) using a cell-based assay measuring SARS-CoV-induced cytopathogenic effect on Vero E6 cells. Ten diterpenoids, two sesquiterpenoids and two triterpenoids were potent inhibitors at concentrations between 3.3 and 10 μ M. The concentrations of the 22 compounds to inhibit 50% of Vero E6 cell proliferation (CC50) and viral replication (EC50), were measured. These phytochemical constituents of EOs were revealed for the first time to display specific and significant anti-SARS CoV effect and thus offer a new way for improvement of anti-SARS-CoV drugs.

The data are important because these types of compounds might also be useful to control other Coronaviruses like the SARS-CoV as well as other enveloped viruses like avian influenza virus and Newcastle disease virus.

The effects of *Nigella sativa*, *Anthemis hyalina* and *Citrus sinensis* EOs on the replication of Coronavirus and the expression of TRP genes family was reported [77].

To evaluate the effect of extracts of extracts on the replication of coronavirus (CoV) and on the expression of TRP genes during Coronavirus infection, HeLa-CEACAM1a (HeLa-epithelial carcinoembryonic antigen-related cell adhesion molecule 1a) cells were inoculated with MHV-A59 (mouse hepatitis virus-A59) was found to be the safe active dose. TCID50/ml (Tissue Culture Infectious Dose that will produce a cytopathic effect in 50 % of the inoculated tissue culture cells) was found for treatments to determine the viral loads. The inflammatory cytokine IL-8 level was found to increase for both 24 and 48 h time points following extract treatment. TRPA1, TRPC4, TRPM6, TRPM7, TRPM8 and TRPV4 were the genes which expression levels changed significantly after extract treatments. The virus load decreased when extracts were added to the CoV infected cells. All the extract treatments had an effect on IL-8 secretion, TRP gene expression and virus load after CoV infection and could be the best candidate in our hands that contains potential treatment molecule(s).

MECHANISMS OF ANTIVIRAL ACTIVITY

With regard to the mechanism of antiviral action, in most cases

where antiviral properties have been evaluated before and after host-cell adsorption, the antiviral action has happened mainly upon treatment of virus particles with EO prior to their addition or adsorption to cell monolayers. This recommends a direct effect of EO on free virus particles rather than an intracellular virucidal activity [57,58,60,67,74].

The site of action has not been known (Figure 5), but most of the viruses used and tested have been enveloped viruses, with the exception of poliovirus, adenovirus and tobacco mosaic virus. Viral envelopes are classically resulting from the membrane of the host cell and have a phospholipid bilayer structure. Since numerous EOs have the ability to interrupt biological membranes, it follows that viral envelopes may also be dislocated by EOs, an argument reinforced by electron micrographs of HSV-1 after treatment with clove or oregano EOs presenting envelope interruption [78].

The antiviral effect of EOs, which are lipophilic by nature, likely act to disrupt or interfere with viral membrane proteins involved in host cell attachment [58].

Isoborneol, an oxygenated monoterpene and a chemical constituent of different EOs, displayed a potent antiviral effect against HSV-1 and exactly inhibited glycosylation of viral proteins [66].

Eugenol, a phenylpropane that represents more than 70% in clove EO, delayed the growth of herpesvirus-induced keratitis in the mouse model [64], and inactivated HSV directly [65].

In opposition to the rising body of *in vitro* results, there are very limited studies of *in vivo* antiviral effect of EOs and their characteristic compounds. *Nigella sativa* (seed oil), was evaluated against murine cytomegalovirus [79], and *Heracleum* spp., *C. stauntonii* [45,80], EOs and cinnamaldehyde [48], were tested against influenza in mouse models.

Clinical investigations in humans are also very restricted. *Melaleuca alternifolia* (tea tree) EO has been tested for the treatment of herpes labialis in a small pilot research with encouraging findings, signifying a decrease in the time to complete healing with the application of *Melaleuca alternifolia* EO topical ointment compared to the positive control [240].

Thus different mechanisms of antiviral activity of different essential oils and compounds of essential oils seem to be present.

De Logu et al. [60], reported an inhibition of herpesviruses replication and prevention of cell-to-cell spread by using *Santolina insularis* EO *in vitro*. However, no antiviral activity was reported throughout the intracellular replication step, which is in agreement to other EOs [46]. In addition, a virus without envelope (adenovirus), was not affected or deactivated by eucalyptus EO due to the nonexistence of a viral envelope [81].

Virucidal activity of essential oils, which are lipophilic by nature, is probably due to disruption of the viral membrane or interference with viral envelope proteins involved in host cell attachment. Although selection of resistant mutants is possible, it has been reported that inactivation of virus by lipophilic EOs is time dependent and that infectious virus remaining after treatment are still sensitive to the EOs making selection of resistant mutants unlikely [74].

- Comparison of Two Animal-to-Human Transmitted Human Coronaviruses: SARS-CoV-2 and SARS-CoV. *Viruses*. 2020; 12: 244.
19. Shanmugaraj B, Malla A, Phoolcharoen W. Emergence of Novel Coronavirus 2019-nCoV: Need for Rapid Vaccine and Biologics Development. *Pathogens*. 2020; 9: 148.
 20. Boldog P, Tekeli T, Vizi Z, Dénes A, Bartha FA, Röst G. Risk Assessment of Novel Coronavirus COVID-19 Outbreaks Outside China. *J Clin Med*. 2020; 9: 571.
 21. Pang J, Wang MX, Ang IYH, Tan SHX, Lewis RF, Chen JP, et al. Potential Rapid Diagnostics, Vaccine and Therapeutics for 2019 Novel Coronavirus (2019-nCoV): A Systematic Review. *J Clin Med*. 2020; 9: 623.
 22. De Clercq E. Antiviral Drugs in Current Clinical Use. *J Clin Virol*. 2004; 30: 115-133.
 23. Chattopadhyay D, Naik TN. Antivirals of Ethnomedicinal Origin: Structure-Activity Relationship and Scope. *Mini Rev Medic Chem*. 2007; 7: 275-301.
 24. Cos P, Vlietinck AJ, Berghe DV, Maes L. Anti-Infective Potential of Natural Products: How to Develop a Stronger in Vitro 'Proof-of-Concept'. *J Ethnopharmacol*. 2006; 106: 290-302.
 25. Gautam R, Saklani A, Jachak SM. Indian Medicinal Plants as a Source of Anti-Mycobacterial Agents. *J Ethnopharmacol*. 2007; 110: 200-234.
 26. Harvey AL. Natural Products as a Screening Resource. *Curr Opin Chem Biol*. 2007; 11: 480-484.
 27. Fierascu RC, Fierascu I, Ortan A, Georgiev MI, Sieniawska E. Innovative Approaches for Recovery of Phytoconstituents from Medicinal/Aromatic Plants and Biotechnological Production. *Molecules*. 2020; 25: 309.
 28. Mickymaray S. Efficacy and Mechanism of Traditional Medicinal Plants and Bioactive Compounds against Clinically Important Pathogens. *Antibiotics*. 2019; 8: 257.
 29. Sharifi-Rad J, Ozleyen A, Boyunegmez Tumer T, Oluwaseun Adetunji C, El Omari N, Balahbib A, et al. Natural Products and Synthetic Analogs as a Source of Antitumor Drugs. *Biomolecules*. 2019; 9: 679.
 30. Anand U, Jacobo-Herrera N, Altemimi A, Lakhssassi N. A Comprehensive Review on Medicinal Plants as Antimicrobial Therapeutics: Potential Avenues of Biocompatible Drug Discovery. *Metabolites*. 2019; 9: 258.
 31. Búfalo MC, Figueiredo AS, De Sousa JPB, Candeias JMG, Bastos JK, Sforcin JM. Anti-Poliiovirus Activity of *Baccharis dracunculifolia* and Propolis by Cell Viability Determination and Real-Time PCR. *J Appl Microbiol*. 2009; 107: 1669-1680.
 32. Mukhtar M, Arshad M, Ahmad M, Pomerantz RJ, Wigdahl B, Parveen Z. Antiviral Potentials of Medicinal Plants. *Virus Res*. 2008; 131: 111-120.
 33. Chouhan S, Sharma K, Guleria S. Antimicrobial Activity of Some Essential Oils—Present Status and Future Perspectives. *Medicines*. 2017; 4: 58.
 34. D'agostino M, Tesse N, Fripiat JP, Machouart M, Debourgogne A. Essential Oils and Their Natural Active Compounds Presenting Antifungal Properties. *Molecules*. 2019; 24: 3713.
 35. Boukhatem MN, Ferhat MA, Kameli A, Kebir HT. Lemon Grass (*Cymbopogon citratus*) Essential Oil as a Potent Anti-Inflammatory and Antifungal Drugs. *Libyan J Med*. 2014; 9: 25431.
 36. Boukhatem MN, Kameli A, Ferhat MA, Mekarnia M. Rose Geranium Essential Oil as a Source of New and Safe Anti-Inflammatory Drugs. *Libyan J Med*. 2013; 8: 22520.
 37. Battistini R, Rossini I, Ercolini C, Gorla M, Callipo MR, Maurella C, Serracca L. Antiviral Activity of Essential Oils Against Hepatitis A Virus in Soft Fruits. *Food Environ Virol*. 2019; 11: 90-95.
 38. Brand YM, Roa-Linares VC, Betancur-Galvis LA, Durán-García DC, Stashenko E. Antiviral Activity of Colombian Labiatae and Verbenaceae Family Essential oils and Monoterpenes on Human Herpes Viruses. *J Essent Oil Res*. 2016; 28: 130-137.
 39. Bouazzi S, Jmii H, El Mokni R, Faidi K, Falconieri D, Piras A, Hammami S. Cytotoxic and Antiviral Activities of the Essential Oils from Tunisian Fern, *Osmunda regalis*. *S Afr J Bot*. 2018; 118: 52-57.
 40. Álvarez DM, Castillo E, Duarte LF, Arriagada J, Corrales N, Farías MA, González, PA. Current Antivirals and Novel Botanical Molecules Interfering With Herpes Simplex Virus Infection. *Front Microbiol*. 2020; 11: 139.
 41. Benencia F, Courreges MC. Antiviral Activity of Sandalwood Oil against Herpes Simplex Viruses-1 and-2. *Phytomedicine*. 1999; 6: 119-123.
 42. Sökmen M, Serkedjieva J, Daferera D, Gulluce M, Polissiou M, Tepe B, et al. *In vitro* Antioxidant, Antimicrobial, and Antiviral Activities of the Essential Oil and Various Extracts from Herbal Parts and Callus Cultures of *Origanum acutidens*. *J Agr Food Chem*. 2004; 52: 3309-3312.
 43. Seidakhmetova RB, Beisenbaeva AA, Atazhanova GA, Suleimenov EM, Pak RN, Kulyyasov AT, et al. Chemical Composition and Biological Activity of the Essential Oil from *Artemisia glabella*. *Pharma Chem J*. 2002; 36: 135-138.
 44. Hayashi K, Kamiya M, Hayashi T. Virucidal Effects of The Steam Distillate from *Houttuynia cordata* and its Components on HSV-1, Influenza Virus, and HIV. *Planta Med*. 1995; 61: 237-241.
 45. Zai-Chang Y, Bo-Chu W, Xiao-Sheng Y, Qiang W. Chemical Composition of the Volatile Oil from *Cynanchum stauntonii* and its Activities of Anti-Influenza Virus. *Coll Surf B Biointerf*. 2005; 43: 198-202.
 46. Bonsignore L, Casu L, Loy G, Deidda D, Genco F. Analysis of the Essential Oil of *Oenanthe crocata* L. and its Biological Activity. *J Essent Oil Res*. 2004; 16, 3: 266-269.
 47. Ögütçü H, Sökmen A, Sökmen M, Polissiou M, Serkedjieva J, Daferera D, et al. Bioactivities of the Various Extracts and Essential Oils of *Salvia limbata* CA Mey. and *Salvia sclarea* L. *Turk J Biol*. 2008; 32: 181-192.
 48. Hayashi K, Imanishi N, Kashiwayama Y, Kawano A, Terasawa K, Shimada Y, et al. Inhibitory Effect of Cinnamaldehyde, Derived from *Cinnamomi cortex*, on the Growth of Influenza A/PR/8 Virus *in vitro* and *in vivo*. *Antivir Res*. 2007; 74: 1-8.
 49. Schnitzler P, Schon K, Reichling J. Antiviral Activity of Australian Tea Tree Oil and Eucalyptus Oil against Herpes Simplex Virus in Cell Culture. *Pharmazie*. 2001; 56: 343-347.
 50. Koch C, Reichling J, Schneeje J, Schnitzler P. Inhibitory Effect of Essential Oils against Herpes Simplex Virus type 2. *Phytomedicine*. 2007; 15: 71-78.
 51. Saddi M, Sanna A, Cottiglia F, Chisu L, Casu L, Bonsignore L, De Logu A. Antiherpesvirus Activity of *Artemisia arborescens* Essential Oil and Inhibition of Lateral Diffusion in Vero Cells. *Ann Clin Microbiol Antimicrob*. 2007; 6: 10.
 52. Sinico C, De Logu A, Lai F, Valenti D, Manconi M, Loy G, Fadda AM. Liposomal Incorporation of *Artemisia arborescens* L. Essential Oil and *in vitro* Antiviral Activity. *Eur J Pharmac Biopharmac*. 2005; 59: 161-168.
 53. Reichling J, Koch C, Stahl-Biskup E, Sojka C, Schnitzler P. Virucidal Activity of a β -Triketone-Rich Essential Oil of *Leptospermum scoparium* (Manuka Oil) against HSV-1 and HSV-2 in Cell Culture. *Planta Med*. 2005; 71: 1123-1127.

54. Farag RS, Shalaby AS, El-Baroty GA, Ibrahim NA, Ali MA, Hassan EM. Chemical and Biological Evaluation of the Essential Oils of Different *Melaleuca* Species. *Phytother Res.* 2004; 18, 1: 30-35.
55. Sivropoulou A, Nikolaou C, Papanikolaou E, Kokkini S, Lanaras T, Arsenakis M. Antimicrobial, Cytotoxic, and Antiviral Activities of *Salvia fruticosa* Essential Oil. *J Agr Food Chem.* 1997; 45: 3197-3201.
56. Allahverdiyev A, Duran N, Ozguven M, Koltas S. Antiviral Activity of the Volatile Oils of *Melissa officinalis* L. against Herpes Simplex Virus Type-2. *Phytomedicine.* 2004; 11: 657-661.
57. Schnitzler P, Schuhmacher A, Astani A, Reichling J. *Melissa officinalis* oil Affects Infectivity of Enveloped Herpes Viruses. *Phytomedicine.* 2008; 15: 734-740.
58. Schuhmacher A, Reichling J, Schnitzler P. Virucidal Effect of Peppermint Oil on the Enveloped Viruses Herpes Simplex Virus Type 1 and Type 2 *in vitro*. *Phytomedicine.* 2003; 10: 504-510.
59. Benencia F, Courreges MC. Antiviral Activity of Sandalwood Oil against Herpes Simplex Viruses-1 and-2. *Phytomedicine.* 1999; 6: 119-123.
60. De Logu A, Loy G, Pellerano ML, Bonsignore L, Schivo ML. Inactivation of HSV-1 and HSV-2 and Prevention of Cell-to-Cell Virus Spread by *Santolina insularis* Essential Oil. *Antiviral Res.* 2000; 48: 177-185.
61. Valenti D, De Logu A, Loy G, Sinico C, Bonsignore L, Cottiglia F, et al. Liposome-Incorporated *Santolina insularis* Essential Oil: Preparation, Characterization and *in vitro* Antiviral Activity. *J Lipos Res.* 2001; 11: 73-90.
62. Garcia CC, Talarico L, Almeida N, Colombres S, Duschatzky C, Damonte EB. Virucidal Activity of Essential Oils from Aromatic Plants of San Luis, Argentina. *Phytother Res.* 2003; 17: 1073-1075.
63. Duschatzky CB, Possetto ML, Talarico LB, Garcia CC, Michis F, Almeida NV, et al. Evaluation of Chemical and Antiviral Properties of Essential Oils from South American Plants. *Antivir Chem Chemother.* 2005; 16: 247-251.
64. Benencia F, Courreges MC. *In vitro* and *in vivo* Activity of Eugenol on Human Herpesvirus. *Phytother Res.* 2000; 14: 495-500.
65. Tragoolpua Y, Jatisatienr A. Anti-Herpes Simplex Virus Activities of *Eugenia caryophyllus* (Spreng.) Bullock & SG Harrison and Essential Oil, Eugenol. *Phytother Res.* 2007; 21: 1153-1158.
66. Armaka M, Papanikolaou E, Sivropoulou A, Arsenakis M. Antiviral Properties of Isoborneol, a Potent Inhibitor of Herpes Simplex Virus Type 1. *Antiviral Res.* 1999; 43: 79-92.
67. Minami M, Kita M, Nakaya T, Yamamoto T, Kuriyama H, Imanishi J. The Inhibitory Effect of Essential Oils on Herpes Simplex Virus Type-1 Replication *in vitro*. *Microbiol Immunol.* 2003; 47: 681-684.
68. Cermelli C, Fabio A, Fabio G, Quaglio P. Effect of Eucalyptus Essential Oil on Respiratory Bacteria and Viruses. *Curr Microbiol.* 2008; 56: 89-92.
69. Wang KC, Chang JS, Chiang LC, Lin CC. 4-Methoxycinnamaldehyde Inhibited Human Respiratory Syncytial Virus in a Human Larynx Carcinoma Cell Line. *Phytomedicine.* 2009; 16: 882-886.
70. Ross SA, El Sayed KA, El Sohly MA, Hamann MT, Abdel-Halim OB, Ahmed AF, et al. Phytochemical Analysis of *Geigeria alata* and *Francoeuria crista* Essential Oils. *Planta Med.* 1997; 63: 479-482.
71. Bishop CD. Antiviral Activity of the Essential Oil of *Melaleuca alternifolia* (Maiden & Betche) Cheel (Tea Tree) against *Tobacco Mosaic Virus*. *J Essent Oil Res.* 1995; 7: 641-644.
72. Meneses R, Ocazonez RE, Martinez JR, Stashenko EE. Inhibitory Effect of Essential Oils Obtained from Plants Grown in Colombia on Yellow Fever Virus Replication *in vitro*. *Ann. Clin. Microbiol. Antimicrob.* 2009; 8: 8.
73. Loizzo MR, Saab AM, Tundis R, Statti GA, Menichini F, Lampronti I, et al. Phytochemical Analysis and *in vitro* Antiviral Activities of the Essential Oils of Seven Lebanon Species. *Chem Biodiv.* 2008; 5: 461-470.
74. Schnitzler P, Koch C, Reichling J. Susceptibility of Drug-Resistant Clinical Herpes Simplex Virus Type 1 Strains to Essential Oils of Ginger, Thyme, Hyssop, and Sandalwood. *Antimicrob Agents Chemother.* 2007; 51: 1859-1862.
75. Jackwood MW, Rosenbloom R, Petteruti M, Hilt DA, McCall AW, Williams SM. Avian Coronavirus Infectious Bronchitis Virus Susceptibility to Botanical Oleoresins and Essential Oils *in vitro* and *in vivo*. *Virus Res.* 2010; 149: 86-94.
76. Wen CC, Kuo YH, Jan JT, Liang PH, Wang SY, Liu HG, et al. Specific Plant Terpenoids and Lignoids Possess Potent Antiviral Activities against Severe Acute Respiratory Syndrome Coronavirus. *J Med Chem.* 2007; 50: 4087-4095.
77. Ulasli M, Gurses SA, Bayraktar R, Yumrutas O, Oztuzcu S, Igci M, et al. The Effects of *Nigella sativa* (Ns), *Anthemis hyalina* (Ah) and *Citrus sinensis* (Cs) Extracts on the Replication of Coronavirus and the Expression of TRP Genes Family. *Mol Biol Reports.* 2014; 41: 1703-1711.
78. Siddiqui YM, Ettayebi M, Haddad AM, Al-Ahdal MN. Effect of Essential Oils on the Enveloped Viruses: Antiviral Activity of Oregano and Clove Oils on Herpes Simplex Virus Type 1 and Newcastle Disease Virus. *Med Sci Res.* 1996; 24: 185-186.
79. Salem ML, Hossain MS. Protective Effect of Black Seed Oil from *Nigella sativa* against Murine Cytomegalovirus Infection. *Int J Immunopharmacol.* 2000; 22: 729-740.
80. Tkachenko KG. Antiviral Activity of the Essential Oils of some *Heracleum* L. Species. *J Herbs Spices Med Plants.* 2006; 12: 1-12.
81. Pour PM, Fakhri S, Asgary S, Farzaei MH, Echeverria J. The signaling pathways, and therapeutic targets of antiviral agents: Focusing on the antiviral approaches and clinical perspectives of anthocyanins in the management of viral diseases. *Front Pharmacol.* 2019; 10: 1207.

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