Antibacterial and Antiviral Activity of Eucalyptus oil: A Systematic Review

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Artikel Review

Abstract: *Eucalyptus sp. is a family member of Myrtaceae, and its oil has been used commercially in the food industry, cosmetics, and pharmaceutical preparation. The fame of Eucalyptus oil rose during the COVID-19 pandemic because several claims have antiviral activity against the coronavirus. Nevertheless, this claim is not scientifically proven and could lead to misinformation among the public. Eucalyptus oil is known to have antibacterial activity against gram-positive and gram-negative bacteria. However, to what extent its effectiveness is has yet to be discovered. Therefore, this study aims to assess eucalyptus oil's antibacterial and antiviral activity using the Cochrane systematic review. The studies included in the systematic review were retrieved from the PubMed and Science Direct databases. The search query was ("Eucalyptus oil" OR "Eucalyptol") AND ("Antibacterial" OR "Antiviral" OR "MIC"). There are 114 articles identified from the search strategies, and additional 4 articles were found from citation research. After the removal of duplication, 83 articles remained. However, 61 articles were excluded because they did not report the antimicrobial activity of eucalyptus oil. Twenty-two articles were screened for full-text, and 61 were excluded because it does not meet the inclusion criteria. Finally, 16 articles were included in this systematic review. Eucalyptus oil has an antibacterial and antiviral activity that depends on its chemical composition and microbial strains. Therefore, make it a prominent candidate as an antimicrobial and disinfectant compound. However, future clinical study about its mechanism of action is needed.*

Keywords: *eucalyptus oil, eucalyptol, antibacterial, antiviral, MIC.*

Abstrak: *Eucalyptus sp.* adalah anggota keluarga Myrtaceae, dan minyaknya telah digunakan secara komersial dalam industri makanan, kosmetik, dan sediaan farmasi. Ketenaran minyak kayu putih naik selama pandemi COVID-19 karena beberapa klaim memiliki aktivitas antivirus terhadap virus corona. Namun demikian, klaim ini tidak terbukti secara ilmiah dan dapat menimbulkan misinformasi kepada publik. Minyak kayu putih diketahui memiliki aktivitas antibakteri terhadap bakteri gram positif dan gram negatif. Namun, sejauh mana efektivitasnya hampir tidak diketahui. Oleh karena itu, penelitian ini bertujuan untuk menilai aktivitas antibakteri dan antivirus minyak kayu putih menggunakan tinjauan sistematis Cochrane. Artikel yang diikutkan dalam tinjauan pustaka sistematis berasal dari database PubMed dan Science Direct. Kata kunci pencarian yang digunakan adalah ("Eucalyptus oil" OR "Eucalyptol") AND ("Antibacterial" OR "Antiviral" OR "MIC"). Strategi pencarian menemukan 114 artikel, dan tambahan empat artikel ditemukan dari penulusuran sitasi. Setelah menghilangkan artikel duplikasi tersisa 83 artikel . Namun, 61 artikel tidak diikutkan dalam tinjauan sistematis karena tidak melaporkan aktivitas antimikroba dari minyak kayu putih. Terdapat 22 artikel yang disaring melalui pembacaan teks lengkap, namun 61 artikel dikeluarkan dari studi karena tidak memenuhi kriteria inklusi. Akhirnya, hanya 16 artikel yang diikutkan dalam tinjauan pustaka sistematik ini. Minyak kayu putih memiliki aktivitas antibakteri dan antivirus yang bergantung pada komposisi kimia dan strain mikroba. Sehingga menjadikannya bahan alam yang dapat digunakan sebagai senyawa antimikroba dan desinfektan. Namun, diperlukan studi klinis untuk untuk mengetahui mekanisme kerja terhadap aktivitas farmakologi ini.

Kata kunci: minyak kayu putih, eucalyptol, antibakteri, antivirus, MIC.

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Introduction

Eucalyptus oil is a clear liquid with a distinctive aroma depending on its origin. It is colorless when refined but is usually slightly yellow when first distilled from the leaves (1). The eucalyptus plant was traditionally used as an antiseptic to treat respiratory tract infections. It can also be used for relaxation, weight loss, treating infections from fungi, and diabetes mellitus in traditional medicine (2,3). Eucalyptus oil is extracted from the eucalyptus plant with various process stages. Eucalyptus comes from the Myrtaceae family, has about 700 species, and among them, about 300 species of *Eucalyptus* sp. have volatile oils. This plant genus originates in Australia and has spread worldwide, including Indonesia. This spreading is possible because the plant is adaptable, easy to cultivate, and has relatively fast growth. Also, Indonesia is a suitable place for the growth of this plant (2,3). Eucalyptus oil contains of 1,8-cineole, (R)-4-methyl-2-pentyl acetate, 3-methylbutanal, α-pinene, β-pinene, Sabinene, Myrcene, and many more. 1,8-cineole is the most abundant constituent in eucalyptus oil (4).

Although arsphenamine was the first antibiotic found, penicillin started the golden age of natural product antibiotic discovery. However, nowadays, there is an antimicrobial resistance crisis due to pathogens' evolution toward drug resistance, such as MRSA (Methicillin-Resistant *Staphylococcus aureus*). Some antimicrobial resistance (AMR) infections currently are not effectively treated. Therefore, it is time to discover new microbial candidates from Natural products (NPs) because these compounds are rich in their chemical diversity and effectiveness as antibiotics (5,6). This search should be continuously conducted because viruses and bacteria constantly develop and mutate. Also, there is a possibility that the antiviral and antibiotics commonly used will be less effective or even ineffective because of microbial resistance. Therefore, discovering an antimicrobial candidate effective against a resistant microbe is essential (7,8).

The fame of eucalyptus oil rose during the COVID-19 pandemic because several claims have antiviral activity against the coronavirus (9). Nevertheless, this claim is not scientifically proven and could lead to misinformation among the public. Eucalyptus oil is known to have antibacterial activity against gram-positive and gram-negative bacteria (10). However, to what extent its effectiveness is hardly known. Therefore, this study aims to assess eucalyptus oil's antibacterial and antiviral activity using a systematic review with the Cochrane method

Materials and Methods

Research Design

This research uses the Cochrane systematic review method to study eucalyptus oil's antibacterial and antiviral activity.

Search Strategy and Selection Criteria

The studies included in the systematic review were retrieved from the Pubmed and Science Direct databases. The search query was ("Eucalyptus oil" OR "Eucalyptol") AND ("Antibacterial" OR "Antiviral" OR "MIC"). The study was conducted in December 2020.

The collected abstract was reviewed, and a study was considered eligible for inclusion if it contains eucalyptus oil MIC and details of the applied MIC methodologies. Selected MIC methodologies were microdilution (BMD) and agar diffusion.

Inclusion criteria: Essential oils extracted from *Eucalyptus sp.* The study contains the antibacterial study of these oils reported as MIC (Minimum Inhibitory Concentration) and inhibition zone. Meanwhile, there are no particular criteria for antiviral activity reports.

This study used no exclusion criteria. The included articles only need to meet the inclusion criteria.

Data extraction

After the title and abstract were screened, four authors independently assessed and analyzed the selected studies.

Data extracted from the identified studies were (1) the source of the eucalyptus oil used in the study; (2) the study design; (3) the experimental methods used for determining the antibacterial and antivirus activity of the oil; (4) the microbial strains used for antibacterial and antivirus determination; (5) results of the

antibacterial and antivirus activity; (6) country where the study was conducted and; (7) the year when the study was reported.

Results and Discussion

There are 114 articles identified from the search strategies, and additional 4 articles were found from citation research. After duplication, 83 articles remained. However, 61 articles were excluded because they did not report the antimicrobial activity of eucalyptus oil. Twenty-two articles were screened for full-text, and 61 were excluded because it does not meet inclusion criteria. Finally, 16 articles were included in this systematic review **(**Error! Reference source not found.**)**.

Eucalyptus oils' source

The source of eucalyptus oil comes from various species. There are 15 species of *Eucalyptus* sp. included in this study; *E. globulus* oil was the most studied **(**Error! Reference source not found.**)**. However, two articles do not mention essential oil sources (11,12). Oils' source is essential because each *Eucalyptus* sp. species will produce oil with a different yield and chemical composition. Thus, it will produce significantly different antimicrobial activity. Moreover, other factors can affect the oil's characteristics, such as the sample's age when harvested, the harvest date (season), chemotype, plant organ, geographical origin, and extraction method (13–15).

Eucalyptus oils' chemical properties

Eucalyptus oil has been used extensively in traditional medicine and written in some pharmacopeia. Moreover, British pharmacopeia, European, and Chinese pharmacopeia stated that Eucalyptus oil for medicinal purposes must contain 1,8-cineole by not less than 70% (14)

Table 1. Source of Eucalyptus oil

Source of Essential Oil	Included in articles
E. bicostata	1
E. camaldulensis	3
E. cinerea	1
E. citriodora	3
E. globulus	9
E. largiflorence	1
E. lehmannii	1
E. leucoxylon	1
E. maidenii	1
E. malliodora	1
E. polycarpa	1
E. radiata	1
E. smithii	1
E.staigeriana	1
Eucalyptus oil commercial	2

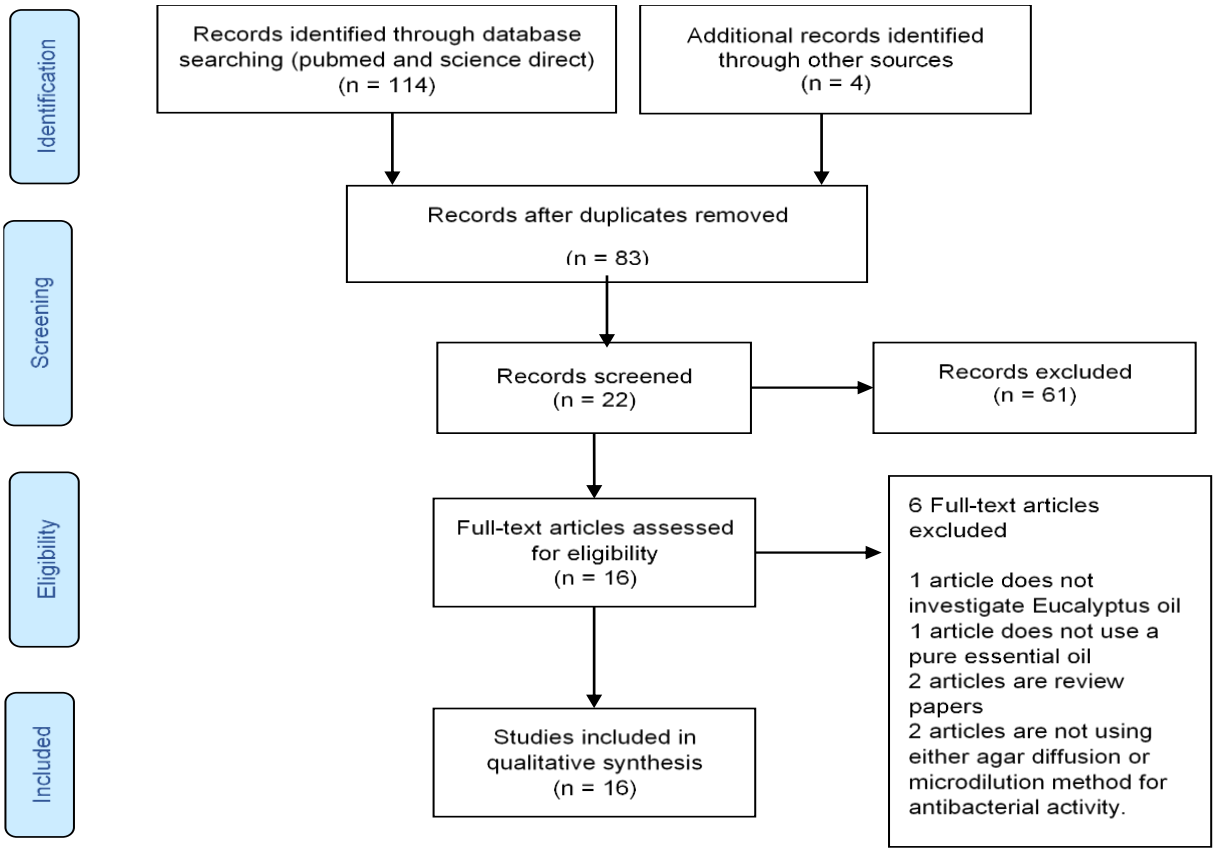

Figure 1. Results of literature research. The literature search was conducted using Cochrane method and the result is displayed in the PRISMA diagram. The search resulted 118 articles, but only 16 articles included in the study.

Although 1,8–cineole, also known as eucalyptol, is a chemical marker, no evidence found in this study shows that it is significantly correlated with eucalyptus oils' antimicrobial activity. Furthermore, antimicrobial activity may arise because of the synergic effect among major and minor chemical components. So, the presence of another compound should be considered.

Eucalyptus oil's chemical profile is reported in eleven studies (13–23). The oils' composition varies among species and also among their origin. A study reported that *E. citriodora* oil containing a low amount of eucalyptol and a high amount of citronellal has the most antibacterial activity among the two species tested (17). Aromadendrene was reported that has a more significant contribution to oils' antimicrobial activity than 1,8-cineole (14). Different oils' compositions will yield different antimicrobial activities. Since essential oils' comprises of several volatile compounds, and also many factors affect oils' composition.

Bacterial strains used in the test

In the study, there are 45 bacterial strains included in this study. MRSA was the most used tested bacteria, followed by *S. aureus*, *P. aeruginosa*, and *K. pneumoniae*. Some studies included clinically isolated microbial strains compared with reference strains (16). Among tested bacteria, *A. burmannii* was reported as the most susceptible gram-negative bacteria (14,16), probably because of the difference in outer membrane from other Enterobacteriaceae (14,17).

Antibacterial activities

All studies reported that eucalyptus oil has antibacterial and antiviral activity against tested bacteria **(**Error! Reference source not found.**)**. Antimicrobial activity is present in both the oil and its vapor (18).

Table 2 Studies included in analysis. A summary of the studies

Source of Eucalyptus oil	Study design	Experimental Methods	Microbial Strains	Result Finding	Country and Study	Study
E. globulus and E. radiata	Experimental	Disc diffusion and Broth microdilution	*P. aeruginosa, E. coli, K. pneumoniae ATCC,* and *A. baumannii*	Eucalyptus oil shows antibacterial activity. *E. radiata* oil shows more antibacterial activity than *E. globulus* oil.	Portugal	Luís et al. 2016 (16)
E. camaldulensis	Experimental	Disc diffusion and broth microdilution	*P. carotovorum, R. solanacearum, Dickeya spp. A*nd *A tumefaciens.*	Eucalyptus oil shows antibacterial activity against the studied plant bacterial pathogen.	Egypt	El Hefny et al. 2017 (23)
E. citriodora folium, E. radiata folium, E. globulus folium and E. globulus fructus.	Experimental	Broth microdilution	MRSA, VRE, *E. coli, P. aeruginosa* and *A. baumannii*	Eucalyptus oil shows antibacterial activity. The most significant activity showed by oil from *E. globulus* fruit.	Germany	Mulyaningsih et al. 2011 (14)
E. globulus	Experimental	Disc diffusion and Broth microdilution	*B. cereus, E. coli., K. pneumonia,* MRSA	Eucalyptus oil shows antibacterial activity against tested bacteria. However, the effect is weaker than the *Thymus vulgaris* oils.	Iran	Tohidpour et al. 2010 (19)
E. globulus	Experimental	Agar well diffusion assay	*S. mutans*	Eucalyptus oil shows antibacterial activity against *S. mutans.*	India	Chaudhari et al. 2012 (24)
NA	Experimental	Disc diffusion assay	*L. buchneri, L. brevis, S. gordonii, S. mutans, S. aureus, S. epidermidi, E. faecium, E. faecalis, P. micra, C. albicans A.actinomycetemcomitans,* and *C. glabrata*	Eucalyptus oil shows antibacterial activity. However, the activity is lower compared with other tested essential oil.	Germany	Karbach et al. 2015 (11)

Source of Eucalyptus oil	Study design	Experimental Methods	Microbial Strains	Result Finding	Country and Study	Study
NA	Experimental	Disc diffusion assay	*P. gingivalis*	Eucalyptus oil shows antibacterial activity. The activity is directly proportional to the oil's concentration.	India	Hans et al. 2016 (12)
E. globulus	Experimental	Disc diffusion assay	*E. coli, S. paratryphi, K. pneumoniae, Y. enterocolitica, P. aeruginosa, A. hydrophila, C. jejuni, E. faecalis,* and *S. aureus*	Eucalyptus oil shows antibacterial activity. The activity depends on the oil's composition and the tested bacterial strain.	Turkey	Ozogul et al. 2015 (20)
E. camaldulensis	Experimental	Agar well diffusion assay	*S. aureus, B. subtilis, E. coli,* and *Streptococcus sp.*	Eucalyptus oil extracted from the leaf and fruit shows antibacterial activity against tested bacteria.	Turkey	Dogan et al. 2017 (21)
E. globulus	Experimental	Disc diffusion assay	*S. aureus, B. subtilis, E. coli,* and *S. intermedius*	Eucalyptus oil shows antibacterial activity. The activity depends on its chemical composition.	Thailand	Chahomchuen et al. 2020 (13)
E. citriodora, E. Smithii, E. Stern	Experimental	Disc diffusion assay	*E. faecalis, B. cereus, L. monocytogenes, S. aureus,* MRSA, *S. tryphimurium, P. aeruginosa, E. coli, K. Pneumoniae, A. baumannii, C. violaceum*	Eucalyptus oil shows antibacterial activity. Oils from E. citriodora and E. staigeriana show the most significant activity. Gram-negative strains are more resistant to essential oil.	Portugal	Luís et al. 2017 (17)
E. globulus	Experimental	Disc diffusion assay	MRSA and *P. aeruginosa*	Eucalyptus oil shows antibacterial activity. However, its activity lower than other essential oil tested.	Hungary	Ács et al. 2016 (18)

Source of Eucalyptus oil	Study design	Experimental Methods	Microbial Strains	Result Finding	Country and Study	Study
E. camaldulensis, E. polycarpa, E. malliodora, and *E. largiflorence*	Experimental	Agar well diffusion and Broth microdilution	*S. aureus*	Eucalyptus oil shows antibacterial activity against *S. aureus*.	Iran	Panahi et al. 2011 (25)
E. globulus	Experimental	Disc diffusion and Broth microdilution	*S. aureus, B. cereus, E. faecalis*	Eucalyptus oils show antibacterial activity. Also, show partial synergic activity with ampicillin against MRSA.	Tunisia	Salem et al. 2018 (15)
E. bicostata, E. cinerea, E. maidenii, E. odorata, E. sideroxylon, E. lehmannii, E. astrigens, and *E. leucoxylon*	Experimental	Disc diffusion assay Broth microdilution Cytotoxicity assay	*H. influenza, K. pneumoniae, P. aeruginosa, S. aureus, S. agalactiae, S. penumoniae, S. pyogenes* and Coxsakievirus B3 Nancy strain	Eucalyptus oil shows antibacterial and antiviral activity. Oils from *E. odorata* show the strongest antibacterial activity, and oils from *E. bicostata* shows the strongest antiviral activity.	Tunisia	Elaissi et al. 2012 (22)
E. polybractea	Experimental	Plaque assay technique	Influenza virus A strain *E. coli* phage M13	Eucalyptus oil aerosols show antiviral activity against Influenza Virus A at the tested condition.	Australia	Usachev et al. 2013 (26)

However, eucalyptus oil's antimicrobial activity is varied significantly within species and microbe strains (13). The antibacterial activity of essential oil is related to their lipophilic profile, enabling them to penetrate the cell and causing cell leakage (16). It has been reported that gram-positive bacteria are more susceptible to essential oil than gram-negative bacteria (15,20) because gram-negative bacteria have an outer membrane layer, which acts as a robust permeability barrier (17).

Compared with other essential oil, eucalyptus oil has lower antimicrobial effects (11,20,24) but has a better effect against several bacteria such as *Porphyromonas gingivalis* (12) and *A. actinomycetemcomitans* (11). Several studies reported that *S. aureus* is a susceptible bacteria toward eucalyptus oil (20,22,25). The eucalyptus oil synergizes with chloramphenicol against the *A. burmannii* strain (16) and ampicillin against MRSA (15). It also shows additional effects with ampicillin against *K. pneumoniae* (15).

Antiviral activities

Two studies reported the antiviral activity of eucalyptus oil (22,26). This finding shows that there are limited studies about the antiviral activity of eucalyptus oil. However, they only reported the oil's antiviral activity against Coxsakievirus B3 when the oil directly contacted the virus (22). It also has antiviral activity against the Influenza A virus but is ineffective against phage M13 (26). This result is similar to antibacterial activity, where its effects depend on virus strains and oils' chemical compounds. Although two reports show that the oil has antiviral activity, a more extensive study with various virus strains is needed to see how broad its antiviral spectrum is.

Limitation

Among the 16 studies included in this study, five studies were performed in Europe (11,14,16–18), seven studies were performed in Asia (12,13,19–21,24,25), three studies in Africa (15,22,23), and one study from Australia (26). Although there were only 16 articles returned in the search, this does not imply that the antimicrobial activity of eucalyptus oil has not been extensively studied. This is due to the study design limitation, which only limited the search for English literature. A similar study was most likely reported in the local language, particularly in the region where eucalyptus oil is widely used.

Conclusion

This study concludes that eucalyptus oil has antibacterial dan antiviral activity. Thus, eucalyptus oil is a prominent alternative to antibiotics or disinfectants. However, further studies are needed to examine its mechanism of action and synergistic effects among the chemical component. For future research, eucalyptus oil's synergic effect with other compounds or antibiotics is needed to study the possibility of eucalyptus oil used in a clinic setting. Also, a study about the antiviral activity of eucalyptus oil is needed.

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