Review

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The Potent Antimicrobial Spectrum of Patchouli: Systematic Review of Its Antifungal, Antibacterial, and Antiviral Properties

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Abstract

Intention towards natural essential oils from medicinal plants has increased rapidly over the past decade as these oils have antimicrobial and antioxidant properties against various chronic diseases. One essential oil source with antimicrobial properties is the essential oil from *Pogostemon cablin* (Blanco) Benth. This review aims to provide information on using patchouli oil as an antimicrobial against bacterial, fungal, and viral pathogens in the last five years. There were 37 articles found in the PUBMED database by June 15, 2023. After searching, 6 of them were duplicates. A total of 2 papers were inaccessible, 4 were not research articles, and five were excluded because they were irrelevant to the scope of this study. This review shows that research related to patchouli as an antimicrobial in the last five years involves *Pogostemon cablin* leaf samples as silver nanoparticle bioreductors. Patchouli oil is used in membrane, nanocomposite film, and starch hydrogel manufacturing. Patchouli oil is a prestigious antimicrobial agent because it can fight numerous pathogenic microbes from bacteria, fungi, and viruses.

1. Introduction

The discovery of antibiotics was a medical advancement, but bacterial resistance accelerated by genetic mutations resulted in rapid resistance. Meanwhile, a new class of antibiotics had not been developed for over three decades [1]. Research on antimicrobial substances using natural resources has become a serious discussion by researchers [2–12]. The utilization of plant secondary metabolites to cure various illnesses was an ancient practice of taking the resources available in markets, gardens, horticulture backyards, and areas with pristine vegetation [10, 13–15].

Essential oils (EOs) are a nature-rich source of bioactive compounds [16]. It has been shown that EOs from dissimilar plants and plant parts are quite different in chemical compounds and antimicrobial characteristics [16, 17]. Interest in EOs and their use is steadily increasing, especially in the medical, cosmetic, and culinary industries [1]. Steam distillation can obtain EOs from different plant materials (leaves, buds, fruits, flowers, herbs, branches, bark, wood, roots, and seeds). EOs are conventionally extracted by steam distillation from plant biomass, which includes dry, unfermented leaves. One type of EO that has antimicrobial properties is EO from *Pogostemon cablin* (Blanco) Benth. Antifungal testing on 12 essential oils showed patchouli oil (PO) was one of the four most effective essential oils against pathogenic fungi [18].

P. cablin is an aromatic blossoming herb in the Lamiaceae known as "patchouli" or "nilam" in Indonesian. Aceh Province is the largest supplier of patchouli worldwide [19, 20]. This plant is an herbal plant that people believe to be a therapeutic plant. *P. cablin* contained various biologically active components, including terpenoids, aldehydes, alkaloids, lignin, organic acids, alcohols, phytosterols, flavonoids, and glycosides [21]. This plant was also known as an aphrodisiac because it raises the secretion of the sex hormones estrogen and testosterone, thus supporting the disappearance of sexual fears and sluggish libido [22]. PO was universally used in several industries, including fragrances and cosmetic items such as deodorizers, soaps, and cleaning detergents. Interest in natural EOs from medicinal plants has risen rapidly over the past decade as these oils have therapeutic traits against some chronic diseases [23]. PO is an FDA-cleared flavoring material used in traditional medication to cure colds, fevers, puke, headaches, and upset stomachs for a long time. Some of the disorders can be successfully medicated using PO, which includes aromatherapy, to heal depression and mood stress as well as enhance sexual attraction [21].

This review article is necessary to inform the progress of research on the application of *P. cablin* as an antimicrobial agent from 2019-2023. This review aims to provide updates on the use of *P. cablin, which can be* used directly as a sample or even included as part of the research sample as an antimicrobial. In addition, this study also recapitulates the results of the antimicrobial activity of samples containing *P. cablin* against pathogenic bacteria, fungi, and viruses.

2. Methods

2.1. Search Strategy

This review was performed according to the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA). The literature search was completed on June 15, 2023, in the PubMed database with the terms as follows: antibacterial, antimicrobial, antiviral, and antifungal paired with *Pogostemon cablin* or patchouli, respectively (Table 1). AND is the term used to search for a specific combination of words, and OR- is used to search between two words. Article titles and abstracts were screened first, and articles that did not satisfy the written criteria were deleted. The research articles analyzed were from the last five years.

2.2. Inclusion and Exclusion Criteria

The criteria for inclusion were as follows: (1) Original articles released in the English language; (2) Research reported using samples from PO or *P. cablin* plant; (3) Research related to antibacterial, antifungal, and antiviral samples; (4) Data obtained from grey literature, meta-analyses, and reviews were excluded from the review and (5) Articles that were not 'full access' were excluded. An illustration of PRISMA in this study has been presented in Figure 1.

3. Results

3.1. Data Selection

A total of 37 papers were searched from the PubMed database. Articles were selected after filtering the titles and abstracts from search outcomes based on a selection of eligibility criteria. A total of 7 articles were excluded because they were not freely accessible. After eliminating duplicate documents, out of the remaining 24 accessible articles, 4 were not research articles. A total of 5 papers were excluded because they were not relevant (Figure 1). The included and excluded studies have been presented in Table 2.

Table 1. Literature search.

Keyword	Total of articles
(((((Pogostemon cablin[Title/Abstract]) OR (patchouli[Title/Abstract])) AND (antibacterial[Title/Abstract]))	17
(((((Pogostemon cablin[Title/Abstract]) OR (patchouli[Title/Abstract])) AND (antimicrobial[Title/Abstract]))	10
(((((Pogostemon cablin[Title/Abstract]) OR (patchouli[Title/Abstract])) AND (antifungal[Title/Abstract]))	4
(((((Pogostemon cablin[Title/Abstract]) OR (patchouli[Title/Abstract])) AND (antiviral[Title/Abstract]))	6
Total articles	37

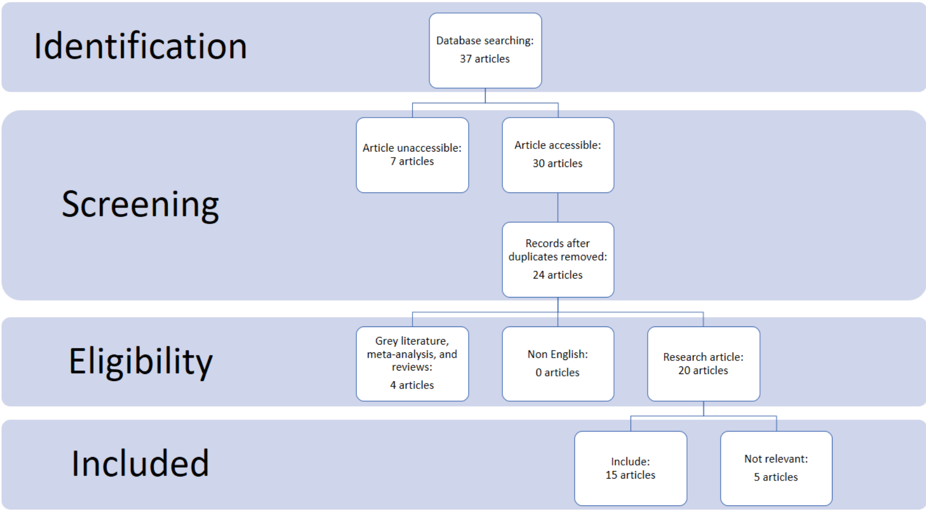

Figure 1. Flow diagram of the search strategy of this study.

Table 2. Details of included and excluded studies.

Included in This Study	Not Relevant	Excluded as not a Research Article
[1], [13], [16], [18], [19], [23], [24], [25], [26], [27], [28], [29], [30], [31], [32]	[33], [34], [35], [36], [37]	[21], [38], [39]

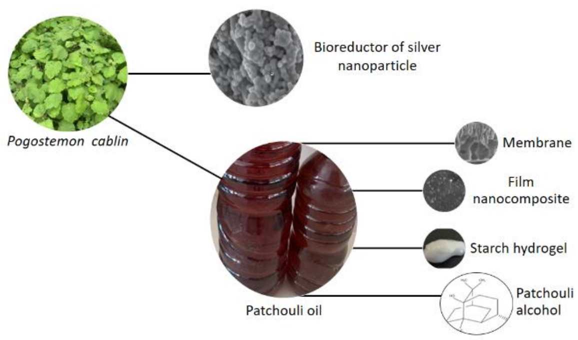

Figure 2. Utilization of patchouli oil in various applications.

3.2. Antifungal, Antibacterial, and Antiviral Activities of Patchouli

Studies on the antimicrobial properties of patchouli in the last five years were of great interest. Various researchers worldwide were making innovations involving patchouli as a sample and part of their samples. The use of patchouli as a subject has been illustrated in Figure 2. The antimicrobial assessment of patchouli has been presented in Table 3.

4. Discussion

P. cablin is a plant that can be found in many countries, such as the Philippines, Indonesia, Malaysia, India, and China [40]. Steam-dried patchouli leaves produce an essential oil called patchouli oil (PO). Patchouli alcohol (PA) is one of the main compounds of *P. cablin*, which belongs to the tricyclic sesquiterpene group with the molecular formula $C_{15}H_{26}O$ [29, 31]. In general, the evaluation of antimicrobial activity of patchouli has been extensively researched in the last five years. The use of patchouli in research samples for antimicrobial investigation has been presented in Figure 2. Research related to patchouli as an antimicrobial in the last five years has directly involved samples in the form of PO [1, 13, 16, 18, 23, 30, 32] as antibacterial and antifungal or PA [24, 29, 31] as antibacterial and antiviral.

PO was reported to have various antifungal activities. PO showed good antifungal performance against six of the eight fungi tested, with the greatest mycelial growth inhibition against *Trichoderma aggressivum* f.sp. *eropaeum* [18]. PO was also reported to have power against *Candida albicans* [30]. The pogostone compound found in PO was reported to have an intense antifungal activity, so wide-scale synthesis of pogostone for the prevention and response to agricultural pathogens is highly recommended [32]. The antifungal mechanism by EO initiated by eugenol acts on the cell membrane through inhibition of ergosterol biosynthesis, which disrupts the integration and function of the fungal cell membrane [41].

PA was considered to be the vital antibacterial component of *P. cablin* [28]. Seven new sesquiterpenoid guaiane and seco-guaiane isolated from PO showed no activity against Methicillin-resistant *Staphylococcus aureus* (MRSA) (ATCC 43300), *Staphylococcus aureus* (ATCC 25923), or *Escherichia coli* (ATCC 25922) (minimum inhibitory concentration> 500 μM) [30]. It was also reported by [24] that PA has activity against some

Table 3. The progression of antimicrobial research involves samples from patchouli.

Sample	The Tested Microbes	Microorganism Test Target	Method	Result	Ref
PA	Bacteria	*Escherichia coli* ATCC 25922 and *Staphylococcus aureus* ATCC 25923, *Klebsiella pneumoniae* ATCC 700603, *Streptococcus pneumoniae* ATCC 49619, *Staphylococcus epidermidis* ATCC 12228, *Enterococcus faecium* ATCC 33186, *Enterococcus faecalis* ATCC 29212, and *Enterococcus faecalis* (high drug resistance) ATCC 51299.	Agar double dilution method	PA effectively inhibited Gram-negative and Gram-positive bacteria (25-768µ g/mL) (1.5-200µ g/mL).	[24]
AgNP- *P. cablin*	Bacteria	*Staphylococcus aureus* ATCC 25923 and *Staphylococcus epidermidis* ATCC 12228	Disc diffusion method	AgNPs synthesized with a light fraction of PO showed high inhibition zones for *Staphylococcus aureus* (12.13 ± 0.92 mm) and *Staphylococcus epidermidis* (10.14 ± 2.92 mm).	[25]
AgNPs- methanol extract of *P. cablin* leaves	Bacteria	*Bacillus subtilis* (ATCC 29737), *Staphylococcus aureus* (ATCC 700698), *Pseudomonas aeruginosa* (ATCC 15442), and *Escherichia coli* (ATCC 8737)	Disc diffusion method	All bacterial strains were inhibited at a concentration of 300 g/ml. Maximum inhibitory activity was observed against *Bacillus subtilis* (16.0±1.7) followed by *Escherichia coli* (14.3±1.6).	[26]
Starch-based Hydrogels loaded with extracted PO	Bacteria	Gram-positive (*Staphylococcus aureus* and *Bacillus subtilis*) and Gram-negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa)*	Disc diffusion method	The antibacterial activity of *Escherichia coli, Pseudomonas aeruginosa, Bacillus subtilis,* and *Staphylococcus aureus* was 29 mm, 26 mm, and 25 mm and 23 mm, respectively.	[27]
Film nanocomposite incorporated with PO	Bacteria	*Staphylococcus aureus*	Viable colony count method	The logarithmic growth stage of bacteria occurred at 16 hours, and the bacteria began to multiply rapidly. However, the growth of *Staphylococcus aureus* was completely restricted within 48 hours, and the number of bacteria gradually decreased.	[28]
PO	Bacteria	*P. aeruginosa* PAO1 and *Chromobacterium violaceum* 12472	Broth micro dilutions method	The MIC of the sample against the tested strains was 2.5%, and sub-MICs were set at 0.31, 0.62, and 1.25%.	[23]
PO	Bacteria	Fifty isolates of *Staphylococcus* spp.	Disc diffusion and broth microdilution methods	PO was most effective against two strains of *Staphylococcus hemolytic* and *Staphylococcus hominins* (the zone of inhibition was 12.67 mm).	[16]
PO	Bacteria	Staphylococci isolated from pyoderma in dogs. A total of 13 *Staphylococcus pseudintermedius* and 8 *Staphylococcus aureus* strains were investigated.	Disk diffusion method	PO showed MICs ranging from 0.125 to 0.5% v/v (1.2-4.8 mg/mL).	[1]
PO	Bacteria	Two gram-negative bacteria (*Pseudomonas aeruginosa* ATCC 25922, *Escherichia coli* ATCC 8789) and a gram-positive bacterium (*Staphylococcus aureus* ATCC 25922)	Microdilution technique	The sample showed antibacterial activity against all tested bacteria MIC and MBC 62.5 µg/mL.	[13]

Sample	The Tested Microbes	Microorganism Test Target	Method	Result	Ref
The polyethersulfone membrane was modified with Plu and PO	Bacteria	*Escherichia coli* (ATCC 25922)	Disc diffusion method	The number of colonies was significantly reduced from 360 to 36 colonies after adding 3% PO to polyethersulfone.	[19]
PO	Fungi	Fungi Isolated from *Panax notoginseng* (Seven fungi: (1) *Fusarium oxysporum*, (2) *Fusarium solani*, (3) *Cylindrocarpon destructans*, (4) *Pythium aphanidermatum*, (5) *Botrytis cinerea*, (6) *Colletotrichum gloeosporioides* and (7) *Rhizoctonia solani*.)	Oxford cup method	PO showed the most potent inhibitory effect on *Colletotrichum gloeosporioides*, with a 100% inhibition rate, followed by *Rhizoctonia solani* (84.44%), *Botrytis cinerea* (82.49%) and *Fusarium oxysporum* (61.97%). However, for *Fusarium solani*, *Cylindrocarpon destructans*, and *Pythium aphanidermatum,* the inhibitory effect was weak, with inhibition rates of 21.01%, 46.93%, and 41.22%, respectively.	[32]
PO	Fungi	*Candida albicans*	Microdilution technique	Two sesquiterpene compounds in the sample showed antifungal activity with MIC values of 500 and 300 μM, respectively.	[30]
PO	Fungi	*Botrytis cinerea, Sclerotinia sclerotiorum, Fusarium oxysporum, Phytophthora parasitica, Pythium aphanidermatum, Alternaria brassicae, Cladobotryum mycophilum* and *Trichoderma aggressivum* f.sp. *europaeum*	Disk diffusion method	PO showed the most outstanding mycelial growth inhibition against *Trichoderma aggressivum* f.sp. *europaeum.*	[18]
PA	Virus	A/Puerto Rico/8/34 (H1N1) strain of influenza A virus	Antiviral cytopathic effect (CPE) Inhibition Assay	PA had a straight inhibitory effect on influenza A viruses.	[31]
PA	Virus	Influenza A virus (IAV)	The plaque assay and immunofluorescence assay. The anti-IAV activities in vivo were determined by mice pneumonia model and HE staining.	PA could block the replication of influenza A virus and H1N1 pandemic virus (Vir09) (IC50 < 6.5 μg/ml).	[29]

Gram-negative bacteria, such as *Enterobacter cloacae, Pseudomonas aeruginosa,* and *Acinetobacter lwoffii* with MIC, 50 µg/mL for each, but no activity was observed against *Klebsiella pneumonia* and *Escherichia coli*. Various species of Staphylococcus bacteria were tested, and there was not a single species that PA could not inhibit, and even PA was active against MRSA [24]. PA was more active against Gram-positive than Gram-negative bacteria [16, 24]. In vivo studies also showed PA could successfully protect mice that were fully infected with MRSA at 100 and 200 mg/kg [24].

PA was known to have anti-influenza A activity, which effectively inhibited PI3K and Akt protein phosphorylation in mice IAV-infected cells [29, 31]. PI3K stands for phosphoinositide 3-kinase, an enzyme crucial in various cellular signaling pathways. It plays a vital role in regulating cell growth, proliferation, differentiation, and survival. AKT protein, also known as protein kinase B (PKB), is a group of proteins that regulate critical cellular functions such as growth and survival. PA significantly inhibits the multiplication of different anti-influenza A virus (IAV) strains in vitro and can block IAV infection by directly deactivating virus particles and interfering with several early stages after virus adsorption [29]. Based on in-depth research, it was known that PA blocked virus replication during the preliminary life cycle stage of influenza A virus infection and explicitly prevented the expression of viral proteins, hemagglutinin (HA), and nucleoprotein (NP) [31]. HA supports influenza virus replication, helps facilitate virus binding to host cell receptors, and induces virus fusion. At the same time, NP is a protein that plays a central role in virus replication [31]. PA affects four nucleotide sites after binding to the influenza A virus, thereby reducing viral activity [31]. Intranasal application of PA has significantly improved mice's survival, effectively indicating that PA can protect cells from virus-induced cell death [29].

The use of patchouli as part of research samples was also reported. One of them is using *P. cablin* leaves as a bioreductor in the green synthesis reaction of silver nanoparticles (AgNP) [26]. Many experts often choose the green synthesis method of AgNPs because of its several advantages, including producing improved antibacterial activity, as well as being cheap and environmentally friendly [42]. AgNPs synthesized using *P. cablin* leaves were obtained in monodispersed, spherical form with smooth edges of different particle sizes with an average size of 25 nm [26]. Interestingly, the plant extract could not inhibit the pathogenic growth of *Staphylococcus aureus* and *Pseudomonas aeruginosa*. However, all bacterial strains were inhibited by AgNP obtained at a concentration of 300 g/ml. Maximum inhibitory activity was observed against *Bacillus subtilis* (16.0 ± 1.7), followed by *Escherichia coli* (14.3 ± 1.6) [26]. The general mechanism of antibacterial AgNPs is breaking the bacterial cell wall membrane. AgNP is uniquely capable of causing dysfunction of bacterial DNA and proteins through interaction with phosphorus or sulfur groups and inducing apoptosis of bacterial cells by generating reactive oxygen species (ROS) and free radicals [43]. Some other possible antimicrobial mechanisms of plant-based AgNP are inhibition of cellular respiration, destabilization of the outer membrane, disruption of proton motive force, and the higher surface volume ratio of AgNP [26].

Another study also purified PO using a rotary evaporator to obtain light and high fractions of PO [21]. The light and high fractions were fractionated at 60°C-65°C and 115°C-160°C, respectively [21]. Research about PO in the world of nanoparticles has also developed to fabricate nanocomposite films based on the combination of poly (vinyl alcohol) and chitosan (PVA/CS). This film nanocomposite consisted of PO-containing silica nanoparticles with a size of 50 nm uniformly dispersed in a micro-porous matrix of PVA/CS film reported to produce durable antibacterial wound dressing substance with improved mechanical and moisturizing qualities [28]. PO was first loaded into a starch-carbopol hydrogel and tested for antibacterial performance [27]. Hydrogels are materials that crosslink physically and/or chemically macromolecules of the same or different substances, forming a 3D network capable of retaining other water volumes without destruction [44]. Pure starch hydrogels showed no antibacterial activity, while starch-carbopol hydrogels with PO showed inhibitory activity on pathogenic bacteria, especially Gram-negative bacteria [27]. The thick peptidoglycan layer, which makes it difficult for the oil to penetrate the bacterial cells, was the cause of this finding [27].

5. Conclusions

Generally, the evaluation of the antimicrobial activity of patchouli was still extensively researched. Research related to patchouli as an antimicrobial in the last five years involved *P. cablin* leaf samples as AgNP bioreductors. In addition, *P. cablin* essential oil in PO was involved in manufacturing membranes, nanocomposite films, and starch hydrogels. Some studies also purified PO and isolated PA as antibacterial and antiviral. In the last five years, there have been no studies of PO against viral pathogens and no antifungal studies of PA. Patchouli was found to have anti-influenza A activity and was more active against Gram-positive than Gram-negative bacteria. PO was also reported to have good antifungal ability, making it one of the opportunities in agricultural disease control.

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