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A Study of Essential Oils from Patchouli (*Pogostemon cablin* Benth.) and Its Potential as an Antivirus Agent to Relieve Symptoms of COVID-19

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Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a new type of virus that attacks the respiratory system and has caused the global epidemic of coronavirus disease 2019 (COVID-19). Some persons who are infected with this virus develop symptoms ranging from a typical cold to fever to more severe illnesses, such as Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS). The development of a SARS-CoV-2 vaccine is being actively researched but will likely take more than a year to become available to the general public. As a result, numerous researchers are actively extracting the components of active chemicals in herbal plants with antiviral potentials, such as patchouli (*Pogostemon cablin* Benth.). Patchouli essential oil, found in this *Lamiaceae* plant, has a wide range of effects, including antibacterial, antifungal, antioxidant, antimutagenic, anticancer, anti-inflammatory, and aromatherapy. More than 140 chemicals have been isolated and identified from the patchouli plant, including terpenoids, phytosterols, flavonoids, organic acids, lignins, alkaloids, glycosides, alcohols, and aldehydes. Patchouli essential oil is mainly composed of sesquiterpene molecules, most of which are patchouli alcohol. Essential oils derived from herbal plant extracts have also been shown to be potent antiviral agents against various viruses. The efficacy of patchouli essential oil, as well as its potential as an antiviral agent to treat SARSCoV-2, will be investigated in this review.

Keywords: patchouli oil, peel-off mask, Staphylococcus aureus bacteria

1. INTRODUCTION

Severe Acute Respiratory Syndrome (SARS) cases continue to dominate the news in much of the world's media. People are becoming increasingly concerned as the number of patients continues to rise, even though no viable treatment to cure the virus's infections has yet to be discovered. WHO has assigned 11 laboratories to examine the virus's emergence, including the National Institute of Infectious Diseases (NIID) in Tokyo and the Centre for Disease Control and Prevention (CDC) in Atlanta (Zu et al. 2020). The cause was initially thought to be the *Chlamydia bacterium* by Chinese experts. Researchers from Hong Kong and other nations, on the other hand, believe there are two possible causes: *Coronavirus* and *Paramyxovirus* (Singhal 2020). WHO ultimately announced that SARS was caused by the Corona Virus, which is now known as SARS-CoV-2, after a long period of investigation.

The coronavirus disease that emerged in 2019 (COVID-19) is characterized by respiratory system disorders, ranging from mild symptoms such as flu to lung infections, such as pneumonia (He et al. 2020). The first case of this disease occurred in Wuhan, China, at the end of December 2019. After that, COVID-19 spread between humans very quickly and spread to dozens of countries, including Indonesia, in just a few months. The spread of the Corona Virus can occur through droplets when the virus carrier coughs, sneezes, or talks. WHO announced that the Corona Virus spreads through small particles that float in the air.

Herbal plants have been identified and have compounds that are useful in preventing or treating disease and perform specific biological functions. About 15 thousand compounds have been isolated from various medicinal plants globally. However, this amount is only ten percent of the total number of compounds extracted from all medicinal plants. One of them is patchouli (*Pogostemon cablin* Benth.) which is one of the essential oil-producing plants that have many health benefits (Isnaini et al. 2022). Patchouli oil contains hydrocarbon compounds in sesquiterpenes (40-45%) and oxygenated hydrocarbon groups (52-57%). The highest content in patchouli oil is patchouli alcohol (patchouli alcohol). Patchouli oil is reported to have many benefits, including antibacterial, antifungal, anti-inflammatory, and antiviral (Risnawaty et al. 2017). Based on the results of this study, it will be studied further regarding patchouli oil and its potential to reduce SARS-CoV-2.

2. PATCHOULI PLANT

Patchouli is a *Lamiaceae* plant with fibrous roots and stem diameters ranging from 10 to 20 nm. After six months, the plant can attain a height of 1 meter and a branch-wide radius of 60 cm—genetic type, cultivation, and habitat all impact patchouli oil content and quality. Patchouli plants thrive in temperatures ranging from 24 to 28 ^oC, with a humidity level of 75 percent. Patchouli plants need much sun to thrive, but they can also thrive in the shade. Patchouli's alcohol concentration is highly influenced by the amount of sunlight it receives, and in shaded places, it is usually low. Drought is also said to be a problem for patchouli plants.

Based on its characteristics, there are three types of patchouli growth in Indonesia, which are, Aceh patchouli (*Pogostemon cablin*), soap patchouli (*Pogostemon hortensis*), and Javanese patchouli (*Pogostemon heyneanus*). The three types of patchouli have different morphology, patchouli alcohol content, oil quality, and resistance.

2.1 Aceh Patchouli (*Pogostemon Cablin*)

Aceh patchouli is a variety of patchouli that rarely blooms yet has a wide distribution and is grown chiefly by patchouli farmers. Aceh patchouli has a significant greater oil concentration and quality than soap patchouli and Javanese patchouli. Aceh patchouli has a smooth leaf surface, blunt serrated leaves, and pointy leaf tips. Depending on the size of the patchouli, it contains 2 to 5% essential oil. Three superior Aceh patchouli varieties have been reported to have high oil content and quality are the variety of Sidikalang, Tapak Tuan and Lhokseumawe (Nuryani 2006). The variety of Sidikalang has higher resilience to bacterial wilt disease (*Ralstonia solanacearum*), the variety of Tapak Tuan patchouli has more patchoulol content, and the variety of Lhokseumawe patchouli has a higher oil content. Nasrun et al. (2004) discovered that compared to Sidikalang patchouli, Tapak Tuan and Lhokseumawe patchouli had meager resistance to bacterial wilt disease. Patchouli from Sidikalang is also resistant to nematodes, parasitic insects that attack plant roots (Mustika and Nuryani 2006). However, the resistance of the three patchouli varieties was weak against budok disease (Wahyuno and Sukamto 2010). Details characteristics of the patchouli variety of Sidakalang, Tapak Tuan and Lhokseumawe are listed in Table 1.

2.2 Patchouli Soap (*Pogostemon hortensis*)

Soap patchouli is another non-flowering patchouli variety. Patchouli of this sort can only be found in Banten and may be used as soap for washing clothing. Patchouli soap contains a little oil, roughly 0.5 to 1.5 percent. Patchouli soap is likewise less attractive on the market due to its poor oil quality.

2.2 Javanese Patchouli (*Pogostemon heyneanus*)

Javanese Patchouli, also known as forest patchouli, is a variety of patchouli that blooms and grows wild in the woods of the island of Java. Although Javanese patchouli has a wider plant structure than Aceh patchouli, it has an oil concentration ranging from 0.5 to 1.5 percent and is less appealing to growers. Javanese patchouli is more prone to nematodes and bacterial wilt disease than Aceh patchouli in disease resistance. Furthermore, it has been discovered that Javanese patchouli is more resistant to fungi-caused budok illness (Wahyuno and Sukamto 2010).

Table 1. Characteristics of Patchouli Variety of Sidakalang, Tapak Tuan and Lhokseumawe

Parameter	Superior patchouli varieties		
	Sidikalang	Tapak Tuan	Lhokseumawe
Leaf color	purplish-green	Green	Green
Leaf length (cm)	6,30-6,45	6,47-7,52	6,23-6,75
Leaf thickness (mm)	0,30-4,25	0,31-0,78	0,31-0,81
Leaf width(cm)	4,88-6,26	5,22-6,39	5,16-6,36
Oil content (%)	2,23-4,23	2,07-3,87	2,00-4,14
Patchouli alcohol content (%)	30,21-35,20	28,69-35,90	29,11-34,46

Source: Nuryani (2005)

3. PATCHOULI PLANT CHEMICAL COMPOSITION

3.1. Volatile Chemical Components

Patchouli essential oil is the principal component extracted from the patchouli plant, and it has a wide range of pharmacological characteristics. In general, the treatment provided to patchouli plants to generate patchouli essential oil might have a qualitative and quantitative impact on its chemical components. It is because patchouli essential oil contains components that are volatile or non-volatile. The volatile chemical components of patchouli oil are presented in Table 2.

Patchouli oil is high in sesquiterpene compounds, particularly patchouli alcohol (patchoulol) a tricyclic sesquiterpene commonly used in perfumes, soaps, and cosmetics. Patchoulena, guaiene, and seychellena are some more sesquiterpene hydrocarbons that contribute to patchouli oil's scent. Based on the literature, patchoulol and α-patchouli are essential components in regulating and controlling the quality of patchouli oil (Donelian et al. 2009, Ramya et al. 2013). Several sesquiterpene compounds with low (minor) levels such as *caryophyllene*, pogostol, α-, β-, γ and δ -*patchoulena*, *seychellena*, *cycloseychellena*, α- and β-*bulnesene*, α- and β-*guaiena*, and norpatchoulenol are also present in patchouli oil (Akhila and Nigam 1984, Akhila et al. 1988). The biological activity of patchouli oil is closely related to its chemical components, such as patchoulol, pogostone, α- and β-patchoulena with chemical structures as shown in Figure 1. Previous studies reported that pogostone is one of the chemical constituents of patchouli oil that is useful for removing intense aromatic odors. Recently, pogostone has been proven to be used in many pharmaceutical activities (Yi et al. 2013, Li et al. 2014).

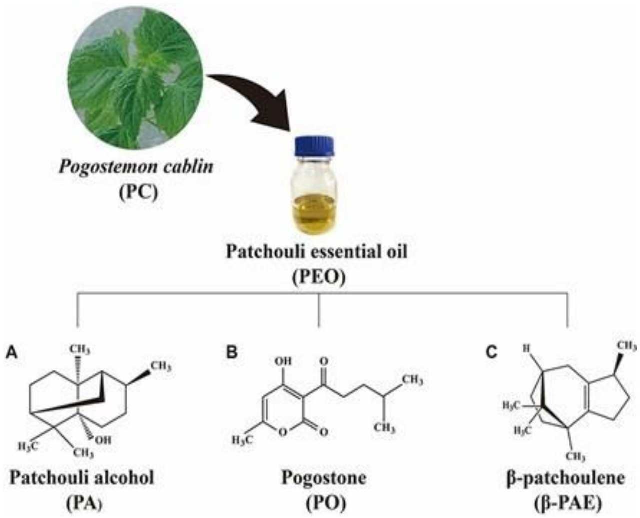

Figure 1. The main components of patchouli essential oil (Hsiao et al. 2019)

Patchouli essential oil has a wide range of chemical compositions, depending on where it was obtained. The sample collection time and the processing procedure impact the volatile oil content of patchouli essential oil. Several studies in the analysis of the chemical composition of patchouli essential oil have been carried out. Aisyah (2010) identified essential oils from Aceh patchouli leaf extract and found five main components, namely patchoulol (32.60%), δ-guiaene (23,07%), α-guiaene (15,91%), seychellene (6,95%), and α-patchoulene (5,47%). Luo et al. (2002) reported that the essential oil content of patchouli leaves (cultivated in Hainan, China) obtained from June to August were 0.8%, 0.7%, and 0.6%, respectively, with the highest patchoulol content. They were obtained in June. Several instruments such as gas chromatography (GC), gas chromatography/mass spectroscopy (GC-MS), and nuclear magnetic resonance (NMR) have been used to identify the chemical composition of patchouli oil from Vietnam. The main compounds identified were α-, β- dan δpatchoulene, β-elemene, β-caryophyllene, α- dan δ-guaiene, seychellene, α-bulnesene, δ-cardinene, pogostol, and patchoulol. Patchoulol content, which ranges from 32-37%, generally smells more like essential oils. However, in the Philippines, it is estimated that there is a distinct aroma of germacrene B, a new sesquiterpene identified as a major component of patchouli oil (Hasegawa et al. 1992).

The essential oil of the patchouli plant collected from China (Gaoyao District, Guangdong Province) and volatile chemical composition were analyzed using GC/MS. The study revealed the presence of pogostone (30.99% in stems, 21.31% in leaves), patchoulol (10.26% in stems, 37.53% in leaves), trans-caryophyllene (4.92% in stems, 60.75% in leaves), α-guaiene (2.27% in stems, 6.18% in leaves) and Seychelles (1.56% in stems, 1.99% in leaves) were the main constituents (Kim et al. 1998). Similarly, GC/MS analysis of patchouli essential oil extracted from the leaves and stems of the patchouli plant obtained from Leizhou County in China showed the presence of sesquiterpene compounds such as patchoulol, α-guaiene, δ-guaiene, α-patchoulene, seychellene, aciphyllene, and trans-caryophyllene (Feng *et al.* 1999).

Table 2. Volatile chemical components in patchouli oil

Compound	Formula	Analysis Method	Reference
Aciphyllene	$C_{15}H_{24}$	GCMS	Feng *et al.* 1999
Aromadendrene	$C_{15}H_{24}$	GC	Kang *et al.* 1998
α- dan β-Bulnesene	$C_{15}H_{24}$	GCMS	Akhila *et al.* 1988
α-Caryophyllene	$C_{15}H_{24}$	GCMS	Akhila *et al.* 1988
Copaene	$C_{15}H_{24}$	GC	Bure dan Sellier 2004
Cycloseychellene	$C_{15}H_{24}$	GCMS	Akhila *et al.* 1988
Elemol	$C_{15}H_{26}O$	GC-TOF MS	Wu *et al.* 2004
Epiglobulol	$C_{15}H_{26}O$	GC-TOF MS	Wu *et al.* 2004
Eucalyptol	$C_{10}H_{18}O$	GC-TOF MS	Wu *et al.* 2004
Farnesol	$C_{15}H_{24}O$	GC-TOF MS	Wu *et al.* 2004
Globulol	$C_{15}H_{26}O$	GC-TOF MS	Wu *et al.* 2004
Guaiene	$C_{15}H_{24}$	GCMS	Wu *et al.* 2004
Gurjunene	$C_{15}H_{24}$	GCMS	Bure dan Sellier 2004
Limonene	$C_{10}H_{16}$	GCMS, GC-TOF MS	Wu *et al.* 2004
Longipinanol	$C_{15}H_{26}O$	GCMS	Hu *et al.* 2006
Patchoulol	$C_{15}H_{26}O$	GC, GCMS, NMR	Hu *et al.* 2006
Patchoulene	$C_{15}H_{24}$	GC, GCMS, NMR	Hu *et al.* 2006
Pinene	$C_{10}H_{16}$	GC, GCMS	Hu *et al.* 2006
Pogostol	$C_{15}H_{26}O$	GC, GCMS, NMR	Akhila *et al.* 1988
Pogostone	$C_{12}H_{16}O_4$	NMR, IR, MS	Hu *et al.* 2006
Selinene	$C_{15}H_{24}$	GC-TOF MS	Hu *et al.* 2006
Seychellene	$C_{15}H_{24}$	GC, GCMS, NMR	Hu *et al.* 2006
Spathulenol	$C_{15}H_{24}O$	GCMS, GC-TOF MS	Wu *et al.* 2004
Valencene	$C_{15}H_{24}$	GCMS	Hu *et al.* 2006
Viridiflorene	$C_{15}H_{26}O$	GCMS	Hu *et al.* 2006

3.2 Non-Volatile Chemical Components

Various phytochemical compounds, including flavonoids, glycosides, triterpenes, sesquiterpenes, lignins, aldehydes, organic acids, and several other components, were found as non-volatile (non-volatile) components of patchouli essential oil. Park et al. (1998) isolated and identified three flavonoids using the fractionation method. The non-volatile compounds identified were licochalcone A, ombuin, and 5,7-dihydroxy-3′,4 -′ dimethoxyflavanone. Amakura et al. (2008) evaluated the quality of Pogostemoni Herba, a crude medication used in Chinese Kampo medicine, using TLC and HPLC methods. They derived a possible chemical marker from the methanol extract of dried patchouli leaves. From this plant, they first extracted three phenylethanoids (isoacteoside, actinoside, and crenatoside). Nine non-volatile chemical compounds were extracted from the methanolic extract of patchouli leaves using column chromatography methods and spectrum data, including epifriedelinol, 5-hydroxymethyl-2-furfural, succinic acid, -sitosterol, daucosterol, 3 -O-methylcrenatoside, crenatoside, isocrenatoside, and apigenin-7-O-β-D-(6 -p-coumaryl)-glucoside (Huang et al. 2009).

4. PATCHOULI PLANT CHEMICAL COMPOSITION

4.1 Antibacterial

In traditional medicine, the patchouli plant treats common cold and fungal infections. Among the ten essential oils studied, patchouli essential oil was more effective in inhibiting 20 bacteria and 12 fungi (Pattnaik et al. 1996). Patchouli essential oil from three geographically different regions (China, India, and Indonesia) was assessed in vitro against 17 pathogenic fungi and 16 commensal bacteria (from skin, mucous membranes, nails, feet, and armpits). Patchouli oil's antifungal and antibacterial action was highly effective (Yang et al. 1996). *Acinetobacter baumannii, Aeromonas veronii, Candida albicans, Enterococcus faecalis, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Salmonella enterica*, and *Staphylococcus aureus* were all inhibited by patchouli essential oil (Hammer et al. 1999). Patchoulol has been proven to have selective antibacterial action against *Helicobacter pylori* without compromising the normal *gastrointestinal flora*. Patchoulol also has urease inhibitory potential and thus can be used as a promising biomolecule to treat H. pylori infection (Yu et al. 2015). In addition, gram-positive bacteria such as *Staphylococcus*, *Bacillus*, and *Streptococcus* species were also successfully inhibited by using patchouli oil (Karimi 2014).

4.2 Antifungal

Candida albicans mycelium is a form of fungus that causes infections of the mouth and skin, and media containing 100 µg/mL a blend of lemongrass, patchouli, thyme, and cedarwood oils is reported to be able to suppress its development (Abe et al. 2003). Patchouli alcohol, found in patchouli oil, exhibits antifungal properties against *Aspergillus* species, according to another research (Kocevski et al. 2013). In addition, *pogostone* which is one of the secondary metabolites in patchouli, is very effective for treating Candida infections, especially for vulvovaginal candidiasis which has been proven by Li et al. (2012). Likewise, patchoulol is able to inhibit *Candida albicans* (Liu et al. 2012) effectively

4.3 Antioxidant

Patchouli essential oil prevents free radicals from oxidizing hexanal to hexanoic acid (Wei and Shibamoto 2007). Patchouli can treat reactive oxygen species, also known as reactive oxygen species (ROS), which cause brain cell harm (Kim et al. 2010). Patchouli essential oil protects human neuroglioma (A172) cells against hydrogen peroxide-induced necrosis and apoptosis, necessitating its use in the treatment of several neurodegenerative illnesses. Patchouli oil prevents photoaging due to its antioxidant properties. It can maintain the skin's structural integrity due to exposure to UV A and UV B rays produced by sunlight (Lin et al. 2014). Patchoulol, on the other hand, boosts UV-induced skin rejuvenation by acting as an antioxidant and anti-inflammatory (Feng et al. 2014). Lipopolysaccharides found on the outer membranes of Gram-negative bacterial cells are also known to induce mastitis. The study conducted by Li et al. (2014) showed that patchoulol was efficient in inhibiting the production of TNF-α, IL-6, and IL-1β.

4.4 Analgesic and Anti-Inflammatory

Analgesic and anti-inflammatory efficacy of patchouli plant methanol extract have been demonstrated in mice (Lu et al. 2011). Plant extracts of *Chrysanthemum Indicum*, patchouli, and *Curcuma wenyuji*n (components of traditional Chinese medicine prescription CPZ) exhibit a strong anti-inflammatory response by regulating interleukin-1β (IL-1β) and prostaglandin E (2). Likewise, patchoulol effectively regulates the mRNA activity of tumor necrosis factor-α (TNF-α), Interleukin1β (IL-1β), Interleukin-6 (IL-6), inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX2) in RAW264.7 cells due to lipopolysaccharide-induced inflammation (Xian et al. 2011). Patchouli oil and ethanolic extracts from its roots and rhizomes also exhibit strong anti-inflammatory properties in vivo (Li et al. 2011, Li et al. 2013). The mechanisms involved in the anti-inflammatory properties of patchoulol have been investigated in mouse macrophages and human colorectal cancer cells (Jeong et al. 2013). Pogostone has an anti-inflammatory effect, according to research by Li et al. (2014), and its potential in creating pharmaceutical medications to treat septic shock has been suggested. Furthermore, by decreasing the action of pro-inflammatory cytokines, the aqueous extract of the patchouli plant can control colon inflammation (Park et al. 2014).

4.5 Antiemetic

Patchouli leaf hexane extract showed antiemetic activity in young chicks. *Patchoulol, pachypodol, pogostol, retusin,* and *stigmast*-4-en-3-one compounds exhibited antiemetic properties at doses of 50–70, 10–50, 20–50, and 50 mg/kg, respectively (Yang et al. 1999).

4.6 Antimutagenic

In *Salmonella typhimurium*, TA1535/pSK1002, the general gene expression due to the SOS response stimulated by the mutagenic agent, 2-(2-furyl)-3-(5-nitro-2-furyl) *acrylamide* was suppressed by the methanol extract of patchouli (Miyazawa et al. 2000).

4.6 Anticancer

5,7-*dihydroxy-3 ,4 -dimethoxyflavanone, ombuin, and licochalcone A′′* compounds were shown to have cytotoxic activity. Research conducted by Park et al. (1998) reported that licochalcone compounds could inhibit phosphoinositide-specific phospholipase C (PI-PLC) gamma 1. Treatment of promyelocytic leukemia cells (HL-60) with licochalcone A compounds induced terminal differentiation with monocyte formation. In addition, patchoulol, the main compound in patchouli essential oil, can inhibit HeLa cell proliferation, suppress cell differentiation, and increase apoptosis in human colorectal cancer cells, HCT116, and SW480 (Yu et al. 2012, Jeong et al. 2013). According to the authors, patchoulol inhibits histone deacetylase two expressions, and histone deacetylase enzyme activity decreases c-myc and activates the NF-κB pathway. Recently, the potential use of patchouli essential oil for antinociceptive and antiallergic activity has been confirmed in mouse models (He et al. 2002).

4.7 Aromatheraphy

Patchouli oil is used in aromatherapy to help relieve stress, insomnia, and anxiety. Its enticing perfume, similar to that of wine, acts as an aphrodisiac and aids in the sharpening of intelligence, attention, and intuition. It is used in spiritual incense to help create a relaxing ambiance. The influence of inhaled scent on sympathetic nervous system activity was examined in humans by measuring catecholamine concentration in serum and monitoring blood pressure variations. The results showed a decrease in sympathetic activity after inhaling the fragrance in normal subjects (Haze et al. 2002). Patchouli essential oil promotes the secretion of adrenal hormones, which helps to alleviate stressrelated weariness and anxiety (Bowles et al. 2002). After inhaling the scent of patchouli oil, physiological reactions such as blood pressure, pulse, stress index, and brain waves (neural oscillations) are lowered. This demonstrates that inhaling the scent of patchouli oil enhances mood and has a therapeutic impact on people. The primary ingredient, patchouli alcohol, is responsible for the odor (Pujiarti et al. 2012).

5. ESSENTIAL OIL FROM PATCHOULI PLANT AS ANTI INFLUENZA

Essential oils derived from herbal plant extracts have been shown to suppress viral infections such as influenza and a variety of other viruses that attack the respiratory system. Influenza is a respiratory infection caused by one of three influenza viruses: type A, type B, and Type C (Glezen and Couch 1997). Influenza viruses that are most significant in human morbidity and mortality are influenza type A viruses found in several species of birds and poultry (Baigent and McCauley 2003). Several different subtypes of influenza A virus have caused global flu pandemics (Guan et al. 2010), including subtype H1N1 which caused the Spanish flu pandemic in 1918 (approximately 40-50 million deaths worldwide) (Johnson and Mueller 2002) and swine flu in 2009 (Schnitzler and Schnitzler 2009), Asian flu 1957–1958 caused by influenza A virus subtype H2N2 (about 1.5 million deaths worldwide) (Schnitzler and Schnitzler 2009), subtype H3N2 causes Hong Kong flu in 1968 (Hsieh et al. 2006), and H5N1 which caused avian influenza in 2004.

There is an interesting study by Vimalanathan and Hudson (2014) evaluating the effectiveness of commercial essential oils from cinnamon (*Cinnamomum zeylanicum*), lemongrass (*Cymbopogon flexuosus*), thyme (*Thymus vulgaris*), bergamot orange *(Citrus bergamia*), and lavender (*Lavandula angustifolia*) against influenza virus type A (H1N1) in vitro. The activity of the essential oil was tested in the liquid phase and the vapor phase at a concentration of 0.3%. The results showed that the essential oils of cinnamon, bergamot, thyme, and lemongrass had 100% inhibition of H1N1 in the liquid phase, while the inhibition of essential oils of lavender was 85%. However, in the vapor phase, 100% inhibition only occurred in essential oil from cinnamon leaves after 30 minutes of exposure. Oils from bergamot, lemongrass, thyme, and lavender have inhibitory properties of 95%, 90%, 70% and 80%, respectively.

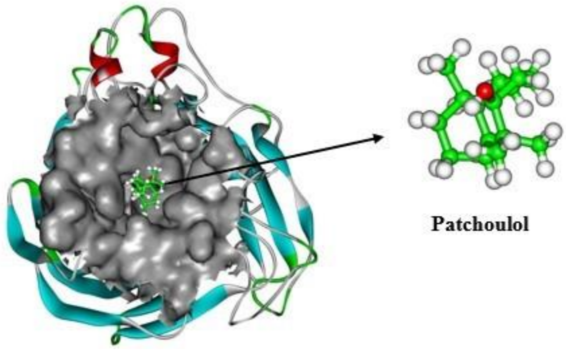

Figure 2. Patchoulol bound to the active site of NA. The surface shape of the NA active site (gray color) was created using the Insightll 2005 script. Patchoulol is represented by a ball and stick model. Band colors: α -helix (red), β -sheet (cyan), turn (green), and random coil (white) (Wu et al. 2011).

Patchouli essential oil has also been reported to have inhibitory activity against the influenza virus. Research conducted by Kiyohara et al. (2012) reported that about 10 g/mL of patchouli leaf methanol extract could inhibit influenza A (H_1N_1) virus up to 99.8% with an IC_{50} value estimated to be 2,6 μM. Another study conducted by Wu et al. (2011) reported the anti-influenza A (H2N2) activity of patchoulol with an IC_{50} of 4 μM. The effect of patchoulol as an anti-influenza was also studied in vivo using mice as a model. The results of this study confirmed that oral administration of patchoulol (20 mg/kg to 80 mg/kg) was able to increase resistance to influenza virus infection by increasing the immune response. Furthermore, it attenuates the systemic inflammatory response. Recently, Wu et al. (2013) observed the effectiveness of patchoulol (10 μg/mL) as an influenza antiviral in vitro and revealed that patchoulol could enhance the ability of the innate immune response and inhibit the performance of the inflammatory factor interferon-alpha (IFN-α) from attenuating the inflammatory response.

The most effective influenza antivirals are *neuraminidase* (NA) inhibitors, which target the NA glycoproteins of influenza A and B viruses. Because the replication of new viruses from infected cells is essential for the influenza life cycle, NA is required to break the α -the ketosidic bond between terminal sialic acid and surrounding sugar residues (De Clercq and Neyts 2007). NA inhibition is done to prevent this cycle by blocking the enzyme's active site, thereby giving the immune system sufficient time to eliminate the infected virus. Patchoulol which is a volatile component of patchouli, is thought to be able to block the role of NA and inhibit influenza virus replication. The binding of patchoulol on the active site of NA is shown in Figure 2. The energy of interaction (E_{inter}) of patchouli alcohol with NA was calculated as -40.38 kcal/mol, where the van der Walls interaction played a more significant role than electrostatic interaction with a contribution of 72% (-29,18 kcal/mol) (Wu et al. 2011). The oxygen atom of the patchouli alcohol interacts with the side chains of the Glu119 and Tyr406 residues, forming one H bond from each residue (Fig. 3). In addition, patchouli alcohol was stabilized by residues Arg118, Asp151, Arg152, Trp178, Ala246, Glu276, Arg292, Asn294 and Gln347 (mainly Asp151, Arg152 and Glu276). The catalytic residues Asp151, Arg152 and Glu276, are essential for NA function and the Glu119 and Tyr406 residues are essential for stabilizing the NA active site. This indicates that the presence of patchouli alcohol will strongly influence the NA function.

6. POTENTIAL OF PATCHOULI ESSENTIAL OIL AS ANTI-SARS-COV-2

Several proteins have been identified that may be potential targets for COVID-19 chemotherapy interventions. These target proteins include the major protease SARS-CoV-2 (SARS-CoV-2 M_{pro}), SARS−CoV−2 endoribonuclease (SARS−CoV−2 Nsp15/NendoU), SARS−CoV−2 ADP−ribose−1″ −phosphatase (SARS−CoV−2 ADRP), SARS−CoV−2 RNA−dependent RNA polymerase (SARS−CoV−2 RdRp), SARS−CoV−2 protein-binding domain (SARS−CoV−2 rS) and angiotensinconverting enzyme in humans (hACE2). SARS CoV-2 M_{pro} is a cysteine protease essential for processing the translated polyprotein of coronavirus RNA, while the non-structural protein 15 (Nsp15) of SARS-CoV-2 is an endoribonuclease that preferentially cleaves RNA in uridylates. Unlike SARS CoV-2 M_{pro} and SARS−CoV−2 Nsp15, ADP ribose phosphatase (ADRP) converts ADP-ribose 1″-monophosphate into ADP-ribose, which helps regulate viral replication. There have been several molecular docking studies on these macromolecular targets. Some carried out molecular docking of natural products with SARS-CoV-2 Mpro (Gentile et al. 2020, Thuy et al. 2020, Joshi et al. 2020, Manish 2020). In addition, commercially available drugs have also been tested using the in-silico method (Beck et al. 2020, Hofmarcher et al. 2020).

A study conducted by da Silva et al. (2020) carried out molecular docking using 171 essential oil components with SARS−CoV−2 M_{pro} (GDP: 5R7Z, 5R80, 5R81, 5R82, 5R83, 5R84, 6LU7, 6M03, and 6Y84), SARS−CoV−2 Nsp15/NendoU (GDP: 6VWW, 6W01, and 6W02), SARS−CoV−2 ADRP, SARS−CoV−2 RdRp (GDP: 6M71), SARS−CoV−2 rS (GDP: 6M0J, 6M17, 6VX1, and 6VW1), and hACE2. The compound with the best-normalized docking score for SARS-CoV-2 M_{pro} was the sesquiterpene hydrocarbon (E)-β-farnesene (DS_{norm} = 115.4 kJ/mol), where DS_{norm} was the docking score normalized for molecular weight. Other essential oil components that showed good docking scores against SARS-CoV-2 Mpro were (E, E)-α-farnesene (DS_{norm} = 115.0 kJ/mol), (E, E) farnesol (DS_{norm} = 112.4 kJ /mol), and (E)-nerolidol (DSnorm = 110.7 kJ/mol). The best docking ligands for SARS−CoV−2 Nsp15/NendoU were (E, E)-α-farnesene (DS_{norm} = 107.5 kJ/mol), (E)-βfarnesene (DS_{norm} = 105.0 kJ/mol), (E, E)-farnesol (DS_{norm} = 104.6 kJ/mol), and (E)-nerolidol (DS_{norm} = 101.6 kJ/mol). (E, E)-Farnesol showed the most exothermic docking to SARS−CoV−2 ADRP. However, the docking energy of (E, E)-α-farnesene, (E)-β-farnesene, and (E, E)-farnesol with the SARS−CoV−2 target is relatively weak, making it impossible to interact with the virus that is the target. Essential oil components, on the other hand, may operate in concert with other antiviral medications, or they may alleviate COVID-19 symptoms (da Silva et al. 2020). We postulated that the components in the patchouli plant had tremendous potential as an antiviral agent to decrease SARS-CoV-2 since the essential oil from the patchouli plant has an inhibitory effect against numerous pathogenic viruses and also includes farnesene and farnesol. However, further research is still needed to prove this.

7. CONCLUSION

Patchouli is being studied worldwide for essential chemical components that might lead to the development of novel medicine molecules with considerable medicinal potential. This study highlights research on patchouli essential oil's phytochemical components and pharmacological actions, as well as its ability to alleviate COVID-19 symptoms. Essential oils have long been recognized to have anti-inflammatory, antibacterial, antioxidant, and antiviral effects, with action against SARS-CoV-2 being suggested. On the patchouli plant, current knowledge bridges the gap between modern scientific investigations and traditional medicinal accounts. Efforts to investigate the pharmacokinetics of patchouli as an antiviral for SARS-CoV-2 have so far shown no conclusive results. However, a molecular docking analysis has been carried out using 171 volatile oil components for the COVID-19 chemotherapy intervention. The best docking ligands for SARS-CoV target proteins are (E, E)-α-farnesene, (E)-β-farnesene, and (E, E)-farnesol. The docking energy of these compounds is still relatively weak and is unlikely to interact with the viral target. Essential oil components in herbal plants, on the other hand, may operate synergistically, whereas essential oils can enhance other antiviral medications or reduce COVID-19 symptoms. Patchouli plants are known to contain farnesene and farnesol. Hence patchouli essential oil may be able to help with COVID-19 symptoms.

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