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A Short Overview of *Curcuma aeruginosa* with Curative Potentials Against COVID-19

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COVID-19 (coronavirus disease) is an infectious disease of the respiratory tract caused by SARS-CoV-2. Nature has provided a great source of antiviral compounds, from which innovative products for the treatment of COVID-19 can be produced. One of the medicinal plants that can be developed for the treatment of COVID-19 is *Curcuma aeruginosa* Roxb. Previous studies have found tracheospasmolytic and anti-inflammatory activity of this indigenous Curcuma species. There are 10 chemical compounds from *Curcuma aeruginosa* that have been proven against COVID-19, namely 1,8-cineole (eucalyptol), α-terpineol, β-caryophyllene, β-eudesmol, β-pinene, β-sitosterol, curcumenol, palmitic acid, succinic acid and zingiberene. Further research is needed for *C. aeruginosa* to become a new antiviral drug for the treatment of COVID-19.

Keywords: *Curcuma aeruginosa*, Chemical compounds, COVID-19.

INTRODUCTION

COVID-19 (coronavirus disease) is an infectious disease of the respiratory tract caused by SARS-CoV-2 or known as coronavirus [1]. China reported its first pneumonia case in Wuhan to the World Health Organization (WHO) on December 31, 2019. The virus was identified as 2019-nCoV on January 7, 2020. WHO named the disease COVID-19 and SARS-CoV-2 for the virus on February 11, 2020 [2,3]. Until the end of 2020, the total number of coronavirus cases in the world reached nearly 83 million people, with more than 1.8 million deaths.

In Indonesia, the first case of COVID-19 was reported on March 2, 2020. There were more than 1.2 million cases in Indonesia, with 33,000 deaths by the middle of February 2021. Common symptoms and signs of COVID-19 infection include fever, cough and shortness of breath. Severe cases of COVID-19 can cause pneumonia, acute respiratory syndrome, kidney failure and even death [4,5]. Most of the infected patients can recover without the need for special treatment. Older adults and people with pre-existing medical conditions such as high blood pressure, cardiovascular disease, or diabetes are more likely to get more serious [6]. With the increasing threat of infection of this virus in humans, the need for new treatment strategies is becoming more evident. There has been no effective vaccine available for COVID-19, so the development of antiviral agents and prevention strategies must be considered. Nature has provided an extraordinary source of antiviral compounds, from which innovative products for the treatment of COVID-19 can be produced [7].

One of the medicinal plants that can be developed for the management of COVID-19 is *Curcuma aeruginosa* Roxb. Previous studies [8,9] have found the tracheospasmolytic effect of antiasthma for *C. aeruginosa*. Further researches found the anti-inflammatory activity of this indigenous Curcuma species [10]. Indonesia is a country with a diverse species of Curcuma. There are about 15 indigenous species of Curcuma found in Indonesia, including *C. aeruginosa* [11]. These plants are in the commodities list which are commonly traded in Indonesia's

traditional market [12,13]. This article overviews the chemical compounds derived from *C. aeruginosa* that can be used against COVID-19.

Morphological properties: *C. aeruginosa* is a native tropical plant from Myanmar and commonly found in Southeast Asia, including Thailand, Malaysia and Indonesia. It is an unexploited perennial herb from the family *Zingiberaceae* [14]. *C. aeruginosa* known as "temu ireng" in Indonesia or "blue pink ginger" in English [15,16]. The traditional use of *C. aeruginosa* in Indonesia is for postpartum treatments, antidiabetic, liver disease, tumor or cancer, appetite stimulant, gastritis, asthma, common cold, cough, dysmenorrhea, intestinal worms, fungal infection, mouth sores, obesity, tonic and rheumatoid problems [11,17,18].

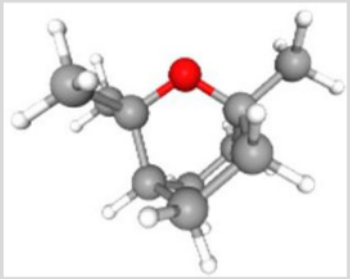
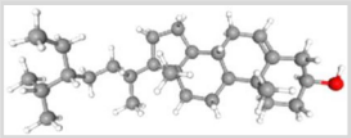
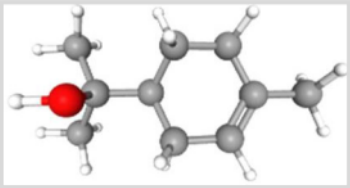
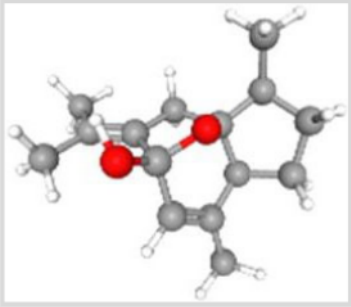
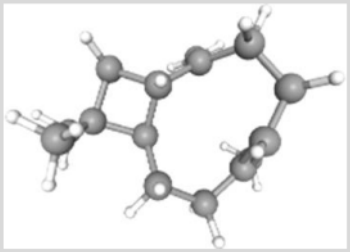
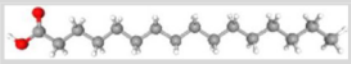
Phytochemical and biological activities: Phytochemical constituents of *C. aeruginosa* are terpenoid, steroid, organic acid, fatty acid, sugar, alkaloid, flavonoid, phenol, glycoside, tannin and saponin [19,20]. Chemically isolated compounds of *C. aeruginosa* are 1,8-cineole (eucalyptol), β-elemene, β-eudesmol, β-pinene, borneol, camphor, caryophyllene, curcumenol, curcumenone, curzerene, curzerenone, cycloisolongifolene, 8,9-dihydro-9-formyl, dehydrocurdione, furanodiene, dihydrocostunolide, furanodienone, furanogermenone, germacrone, isocurcumenol, methenolone, palmitic acid, propiolic acid, sitosterol, succinic acid, terpineol, velleral, (Z)-3-hexenol, Z-α-farnesene, zedoalactone A, zedoalactone B, zedoarol, zedoarondiol and zingiberene [21,22].

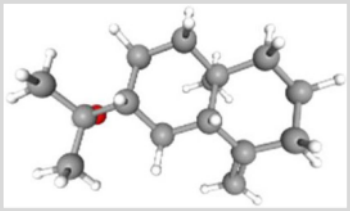
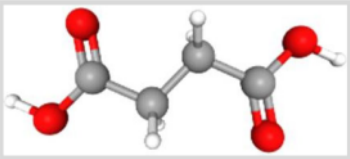
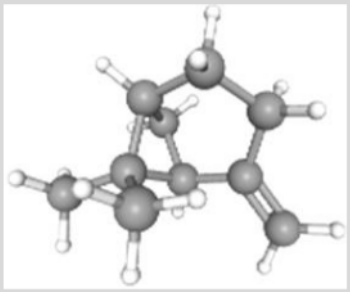
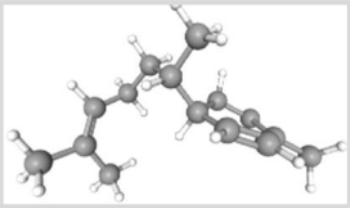
Extracts and essential oils of *C. aeruginosa* show antibacterial activity against *Staphylococcus aureus*, *Streptococcus haemolyticus*, *Streptococcus mutans*, *Bacillus cereus*, *Bacillus subtilis*, *Enterococcus faecalis* [23,24], *Salmonella typhi*, *Escherichia coli* [25], *Pseudomonas aeruginosa*, *Vibrio cholera*, *Klebsiella aerogens*, *K. pneumoniae* and *Serratia marcescens* [14]. The essential oil of *C. aeruginosa* also exhibits antifungal activity against *Candida albicans* and *Cryptococcus neoformans* [26].

Chemical compounds against COVID-19: There are 10 isolated compounds from *C. aeruginosa* (Table-1) have been proven against COVID-19, namely 1,8-cineole (eucalyptol), α-terpineol, β-caryophyllene, β-eudesmol, β-pinene, β-sitosterol, curcumenol, palmitic acid, succinic acid and zingiberene.

Recently, My *et al.* [27] isolated the 1,8-cineole (eucalyptol) from *Melaleuca cajuputi* and conducted the molecular docking against angiotensin-converting enzyme 2 (ACE2) protein in the human body as the host receptor for SARS-CoV-2 and main protease (PDB6LU7) of the SARS-CoV-2. The results show

TABLE-1
LIST OF CHEMICAL COMPOUNDS OF *C. aeruginosa* AGAINST COVID-19 [Ref. 39]

No.	Compound	Structure	No.	Compound	Structure
1	1,8-Cineole (Eucalyptol)		6	β-Sitosterol	
2	α-Terpineol		7	Curcumenol	
3	β-Caryophyllene		8	Palmitic acid	

4	β-Eudesmol		9	Succinic acid	
5	β-Pinene		10	Zingiberene	

that compound have strong interactions with the amino acids of the ACE2 protein and the main protease PDB6LU7 of SARS-CoV2. These natural ingredients can prevent SARS-CoV-2 from entering the human body [27]. Another study reported that 1,8-cineole may interact directly with the COVID-19 viral membrane and decrease the host inflammatory response [7]. 1,8-Cineole is a volatile compound that has been proven to be safe and effective against COVID-19, so it has the potential to be further developed [28].

The molecular docking results of β-eudesmol against the ACE2 protein and the main protease SARS-CoV-2 showed that this compound can prevent SARS-CoV-2 from entering the body [27]. Similarly, compound isolated from Moroccan medicinal plants reported that β-eudesmol can be an inhibitor against SARS-CoV-2 [29]. A molecular docking study was conducted to examine the potential of β-pinene in functional food against COVID-19. β-Pinene shows an affinity for the main protease receptor SARS-CoV-2, thus becoming a SARS-CoV-2 protease inhibitor [30].

β-Caryophyllene was proposed as an herbal candidate with antiviral activity against SARS-CoV-2 using molecular docking [31,32]. Molecular docking study on β-caryo-phyllene as a compound in functional food shows the SARS-CoV-2 protease inhibitor's effect due to its affinity for the primary protease receptor [30]. Another molecular docking results showed that β-caryophyllene has a weak affinity for ACE2 when compared to captopril, which is an inhibitor of this enzyme [33].

Curcumenol extracted from *Solanum tuberosum* and *Brassica juncea* by *in silico* studies is a selective and potent candidate compared to hydroxychloroquine against COVID-19. Molecular docking was carried out on TMPRSS2, PLpro, SARSCoV2 3CLpro, SARSCoVRdRp, SARSCoV2S and ACE2 as SARS-CoV-2 receptors to prevent COVID19 [34]. In another study, palmitic acid was tested against the HSPA5 substrate-binding domain β (SBDβ), the recognition site for the SARS-CoV-2 spike. The molecular docking results showed the affinity of palmitic acid on HSPA5 SBDβ [35].

β-Sitosterol is a chemical compound which is associated with the antiviral signing pathway for COVID-19 [36]. The molecular docking results show that β-sitosterol is an inhibitor of the SARS-CoV-2 central protease receptor [30]. Another molecular docking results showed that β-sitosterol derived from *Tinospora cordifolia* shows an affinity for the 3CLpro receptor, so it can be developed as a drug to fight SARS-CoV-2 [37]. β-Sitosterol also shows a high affinity for the spike glycoprotein and ACE2. This study showed an excellent pharmacokinetic profile with a low level of toxicity [33]. β-Sitosterol in the Shufeng Jiedu capsule used for the treatment of COVID-19 in Traditional Chinese Medicine (TCM) shows a high affinity for the SARS-CoV-2 gene target [38].

The succinic acid has also been proposed as a potential antiviral candidate for the treatment of COVID-19 based on molecular docking results [39]. α-Terpineol also showed a inhibition of ACE2 protein (SARS-CoV-2 receptor host) and PDB6LU7 (main protease SARS-CoV-2). Thus α-terpineol can prevent SARS-CoV-2 invasion into the human body [27]. Meanwhile, zingiberene exhibits significant binding affinity to the ACE2 receptor, so it can be used to inhibit SARS-CoV-2 [33].

Conclusion

Curcuma aeruginosa is one of the indigenous Curcuma species in Indonesia, which can be developed as a treatment of COVID-19. Ten chemical compounds (1,8-cineole (eucalyptol), α-terpineol, β-caryophyllene, β-eudesmol, β-pinene, β-sitosterol, curcumenol, palmitic acid, succinic acid and zingiberene) isolated from *C. aeruginosa* have shown better binding affinity with ACE2 protein and thus inhibit SARS-CoV-2. However, Further research *in vitro* and *in vivo* is much needed for *C. aeruginosa* to become a new antiviral drug for SARS-CoV-2.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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