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IN SILICO ANALYSIS OF ANTIFUNGAL POTENTIAL OF *Centella asiatica* ACTIVE COMPOUNDS AS NATURAL BIOFUNGICIDES FOR OIL PALM FUNGAL DISEASE CONTROL

ANALISIS IN SILICO POTENSI ANTIFUNGI SENYAWA AKTIF *Centella asiatica* SEBAGAI BIOFUNGISIDA ALAMI UNTUK PENGENDALIAN PENYAKIT JAMUR PADA TANAMAN KELAPA SAWIT

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Abstract

This study aimed to analyze the potential of active compounds in pegagan (Centella asiatica) as natural antifungal agents using an in silico approach with PASS Online, SwissADME, and pkCSM. The PASS Online analysis showed that most active compounds of pegagan had antifungal activity probability (Pa) values above 0.5, indicating relatively high biological potential. The compounds with the highest activity were 3-O-beta-D-Glucopyranosyl sitosterol (0.722), Centellin (0.715), Centellicin (0.655), Asiatic acid (0.651), and Kaempferol (0.651). Triterpenoid, flavonoid, and sesquiterpene compounds are known to act through mechanisms including disruption of the fungal cell membrane, inhibition of cell wall synthesis, interference with energy metabolism, and enhancement of oxidative stress in pathogenic cells. SwissADME analysis indicated that the majority of compounds exhibited good solubility, moderate lipophilicity, and bioavailability scores consistent with biological activity. Acetylursolic acid showed the highest bioavailability score of 0.85, while most other compounds ranged between 0.55 and 0.56. The drug-likeness results demonstrated that most compounds complied with Lipinski, Veber, and Muegge rules, indicating their potential as bioactive antifungal candidates. Physicochemical property analysis revealed TPSA values, hydrogen-bond donors and acceptors, and molecular flexibility that support membrane penetration and interactions with fungal biological targets. In addition, pkCSM results showed that most compounds were non-mutagenic, non-hepatotoxic, and exhibited relatively low environmental toxicity. Overall, the results suggest that pegagan has strong potential as a source of environmentally friendly natural antifungal compounds and may be further developed as a biofungicide for controlling fungal diseases in oil palm plants.

Keywords: *pegagan, antifungal, PASS Online, SwissADME, biofungicide*

Abstrak

Penelitian ini bertujuan untuk menganalisis potensi senyawa aktif dalam pegagan (*Centella asiatica*) sebagai agen antifungi alami melalui pendekatan *in silico* menggunakan PASS Online, SwissADME, dan pkCSM. Hasil analisis PASS Online menunjukkan bahwa sebagian besar senyawa aktif pegagan memiliki nilai probabilitas aktivitas antifungi (*Pa*) di atas 0,5, yang mengindikasikan potensi biologis yang relatif tinggi. Senyawa dengan aktivitas tertinggi adalah 3-O-beta-D-Glucopyranosyl sitosterol (0,722), Centellin (0,715), Centellicin (0,655), asam asiatat (*Asiatic acid*) (0,651), dan Kaempferol (0,651). Senyawa golongan triterpenoid, flavonoid, dan seskuiterpena diketahui bekerja melalui mekanisme perusakan membran sel jamur, penghambatan sintesis dinding sel, gangguan metabolisme energi, serta peningkatan

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stres oksidatif pada sel patogen. Analisis SwissADME menunjukkan bahwa sebagian besar senyawa memiliki kelarutan yang baik, lipofilisitas sedang, dan skor bioavailabilitas yang mendukung aktivitas biologis. Asam asetilursolat (*Acetylursolic acid*) menunjukkan skor bioavailabilitas tertinggi sebesar 0,85, sedangkan sebagian besar senyawa lainnya berada pada kisaran 0,55–0,56. Hasil analisis *drug-likeness* menunjukkan bahwa sebagian besar senyawa memenuhi aturan Lipinski, Veber, dan Muegge, yang mengindikasikan potensinya sebagai kandidat senyawa bioaktif antifungi. Analisis sifat fisikokimia mengungkapkan nilai TPSA, donor dan akseptor ikatan hidrogen, serta fleksibilitas molekul yang mendukung penetrasi membran dan interaksi dengan target biologis jamur. Selain itu, hasil pkCSM menunjukkan bahwa sebagian besar senyawa bersifat non-mutagenik, tidak hepatotoksik, dan memiliki tingkat toksisitas lingkungan yang relatif rendah. Secara keseluruhan, hasil penelitian ini menunjukkan bahwa pegagan memiliki potensi yang kuat sebagai sumber senyawa antifungi alami yang ramah lingkungan dan dapat dikembangkan lebih lanjut sebagai biofungisida untuk mengendalikan penyakit jamur pada tanaman kelapa sawit.

Kata kunci: pegagan, antifungi, PASS Online, SwissADME, biofungisida.

INTRODUCTION

Diseases caused by pathogenic fungi are among the major constraints in plantation crop cultivation, including oil palm. Fungal infections can reduce plant productivity, inhibit growth, and cause significant economic losses in the agricultural sector. Synthetic fungicides have long dominated the control of fungal diseases. However, the continuous application of chemical fungicides may cause various negative impacts, such as pathogen resistance, environmental pollution, harmful residues in agricultural products, and disturbances to non-target organisms (Adkar-Purushothama *et al*., 2025). In addition, increasing public awareness regarding food safety and environmental sustainability has encouraged the development of plant-based, natural fungicides as safer and more environmentally friendly alternatives (Khursheed *et al*., 2022).

One of the herbal plants with potential for development as a source of natural biofungicides is *Centella asiatica*. Pegagan is widely known as a medicinal plant containing secondary metabolites, including triterpenoids, flavonoids, saponins, phenolics, and essential oils, which exhibit high biological activity. Several major compounds in pegagan, including asiatic acid, madecassic acid, asiaticoside, kaempferol, and quercetin, are known to exhibit antimicrobial, antioxidant, anti-inflammatory, and antifungal activities against various pathogenic microorganisms (Singh & Singh, 2024). These secondary metabolites have the potential to serve as natural, sustainable inhibitors of fungal pathogens that cause plant diseases.

The triterpenoid compounds in pegagan are known to exert antifungal effects by disrupting fungal cell membrane permeability. Compounds such as asiatic acid and acetylursolic acid can interact with ergosterol in the cell membrane, causing leakage of cellular contents, hyphal damage, and death of pathogenic fungi (Mehta *et al*., 2023). In addition, triterpenoids can inhibit biofilm formation and disrupt microbial cell metabolism. These activities make triterpenoid compounds important candidates for developing botanical fungicides. Recent studies have shown that ursane and oleanane derivatives possess high effectiveness against various plant pathogenic fungi as well as human fungal pathogens (Kim et al., 2018).

Besides triterpenoids, pegagan also contains flavonoids such as kaempferol and quercetin, which are known to possess strong antifungal activity. Flavonoids act through mechanisms involving inhibition of cell wall synthesis, disruption of energy metabolism, and enhancement of oxidative stress in fungal cells. The antioxidant activity of flavonoids also plays a role in inhibiting the growth and development of pathogenic fungal spores (Patil *et al*., 2024). Other studies have explained that flavonoids from herbal plants can work synergistically with other phenolic compounds, thereby enhancing overall antimicrobial and antifungal effectiveness (Cho *et al*., 2026). Therefore, the combination of secondary metabolites in pegagan is predicted to provide a broader spectrum of antifungal activity than using single compounds.

Advances in bioinformatics and computational technology have enabled faster identification of the bioactivity potential of plant compounds through in silico approaches. This method has become an important alternative in pharmaceutical and biotechnology research because it can save time, costs, and laboratory testing materials. One commonly used method is PASS Online, which predicts the biological activity of compounds based on their chemical structures. The probability of activity (Pa) values generated can be used to estimate the potential of compounds as antifungal agents before further in vitro and in vivo testing is conducted (Poroikov *et al*., 2019). The higher the Pa value, the greater the probability that a compound possesses specific biological activity.

In addition to PASS Online, pharmacokinetic analysis with SwissADME is widely used to assess the characteristics of bioactive compounds, including solubility, lipophilicity, bioavailability, and drug-likeness. These parameters are highly important because they influence the ability of compounds to penetrate cell membranes, interact with biological targets, and maintain activity stability. Compounds with good solubility and moderate lipophilicity are generally more effective in inhibiting microbial growth because they can diffuse optimally within biological environments (Chmiel *et al*., 2019). Furthermore, drug-likeness parameters such as the Lipinski, Ghose, Veber, Egan, and Muegge rules are used to predict the suitability of compounds as bioactive candidates based on molecular size, polarity, flexibility, and biological absorption.

The physicochemical characteristics of compounds are also important factors in determining antifungal effectiveness. Parameters such as molecular weight, number of hydrogen-bond donors and acceptors, Topological Polar Surface Area (TPSA), and molecular flexibility influence membrane-penetrating capability and interactions with target proteins in fungal cells. Compounds with TPSA values below 140 Å² generally possess better membrane permeability, resulting in more optimal biological activity (Asano *et al*., 2023). Flavonoids with high numbers of hydroxyl groups are known to enhance affinity toward target biomolecules, thereby improving antifungal activity (Cenobio-Galindo *et al*., 2024).

In addition to biological effectiveness, safety is a major consideration in the development of botanical fungicides. Therefore, toxicity analysis using pkCSM is required to predict the safety of compounds toward living organisms and the environment. Parameters such as AMES toxicity, hepatotoxicity, and environmental toxicity can provide preliminary information regarding the mutagenic potential, liver toxicity, and environmental impacts of bioactive compounds. Plant secondary metabolites with low toxicity are considered safer and have greater potential to be

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Vol. 3, No. 2, Thn. 2026
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developed as environmentally friendly biofungicides than conventional synthetic fungicides. Furthermore, natural compounds are generally more easily degraded in the environment, thereby minimizing the risk of soil and water contamination (Geetha *et al*., 2025).

Based on these potential targets, this study was conducted to analyze the antifungal activity of active compounds in pegagan using an in silico approach with PASS Online, SwissADME, and pkCSM. This analysis is expected to provide information regarding the bioactivity potential, pharmacokinetic characteristics, drug-likeness, physicochemical properties, and toxicity of active compounds in pegagan as natural biofungicide candidates. The results of this study are expected to support the development of safer, more effective, and sustainable botanical fungicides for controlling fungal diseases in oil palm plants.

RESEARCH METHODS

This study employed a descriptive, exploratory approach using an in silico approach to analyze the potential antifungal activity of active compounds from *Centella asiatica* as candidates for natural biofungicides. The in silico approach was selected because it can accelerate the identification of bioactive compounds through computational simulations, with lower cost and time than conventional experimental methods. In addition, this method is widely used in modern medicinal plant bioactive compound development research because it can provide preliminary information regarding the bioactivity, pharmacokinetics, and toxicity of compounds comprehensively (Aware *et al*., 2022).

1. Identification of Active Compounds

The active compounds of pegagan were identified from the literature, including various scientific journals and phytochemical databases. The analyzed compounds included asiatic acid, madecassic acid, asiaticoside, kaempferol, quercetin, and acetylursolic acid, which belong to the triterpenoid and flavonoid groups. The chemical structures of each compound were obtained in Simplified Molecular Input Line Entry System (SMILES) format through the PubChem chemical database. Compound selection was based on recent research reports indicating that pegagan contains secondary metabolites with high biological activity, including antioxidant, antimicrobial, and antifungal properties (Putri *et al*., 2026).

2. Biological Activity Prediction Using PASS Online

Biological activity prediction was conducted using the online platform PASS Online by inputting compound structures in SMILES format. The analysis was performed to obtain the Probability of Activity (Pa) and Probability of Inactivity (Pi) values for antifungal activity. Compounds were considered potentially active when the Pa value exceeded the Pi value. The higher the Pa value, the greater the probability that a compound possesses specific biological activity. Structure-based biological activity prediction approaches have been widely used in modern pharmaceutical and biotechnology research because they can rapidly and accurately predict compound activity prior to further laboratory testing . In addition, secondary metabolites

https://jurnal.rocewisdomaceh.com/index.php/roce e-ISSN : 3032-4505
Vol. 3, No. 2, Thn. 2026
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of pegagan, such as triterpenoids and flavonoids, are known to possess broad biological activities against pathogenic microorganisms (Yanthi *et al*., 2022).

3. Physicochemical and Pharmacokinetic Property Analysis Using SwissADME

Physicochemical and pharmacokinetic property analyses were carried out using the SwissADME platform. The observed parameters included molecular weight, lipophilicity (LogP), number of hydrogen bond donors and acceptors, Topological Polar Surface Area (TPSA), water solubility, molecular flexibility, and bioavailability. In addition, drug-likeness evaluation was conducted based on Lipinski, Ghose, Veber, Egan, and Muegge rules. This analysis is important because the physicochemical characteristics of compounds influence membrane penetration capability, biological absorption, and interactions with target proteins in fungal cells. Compounds with low TPSA values and moderate lipophilicity generally possess better membrane penetration capability, resulting in more optimal biological activity (Ouassaf *et al*., 2023). Pegagan flavonoids and triterpenoids are also known to possess pharmacokinetic characteristics that support their biological activities as natural antimicrobial agents (Andriyanto *et al*., 2026).

4. Toxicity Prediction Analysis Using pkCSM

Toxicity prediction was conducted using the pkCSM platform by inputting compound structures in SMILES format. The analyzed toxicity parameters included AMES toxicity, hepatotoxicity, Tetrahymena pyriformis toxicity, and minnow toxicity. This analysis aimed to evaluate the safety levels of compounds toward living organisms and the environment. Compounds with low toxicity levels are considered safer and have the potential to be developed as environmentally friendly biofungicides. Recent studies have shown that plant secondary metabolites generally possess higher biodegradability and lower environmental pollution risks compared to conventional synthetic fungicides (Mungwari *et al*., 2025).

5. Data Analysis

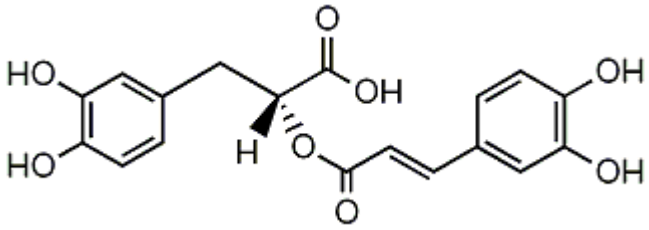
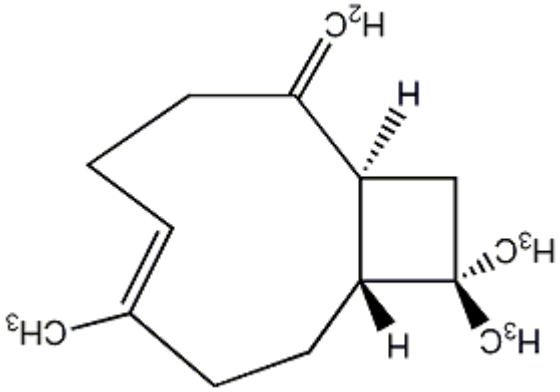
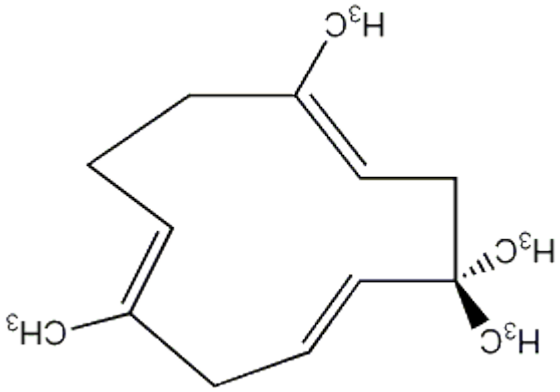
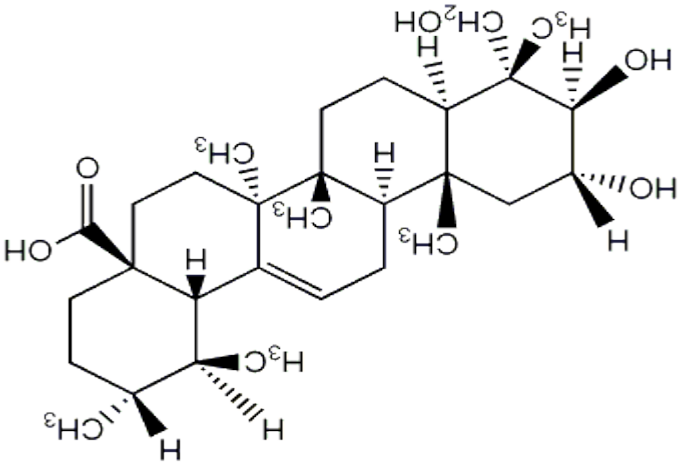
The prediction data obtained from PASS Online, SwissADME, and pkCSM were analyzed descriptively and comparatively. Biological activity values, physicochemical parameters, pharmacokinetic characteristics, and toxicity profiles were compared among compounds to identify the pegagan compounds with the best antifungal potential. The analysis results were then presented in tables and interpreted in light of previous studies on the activity of pegagan secondary metabolites. This comparative approach was used to identify bioactive compound candidates that are effective, safe, and potentially developable as natural biofungicides for oil palm plants.

RESULTS AND DISCUSSION

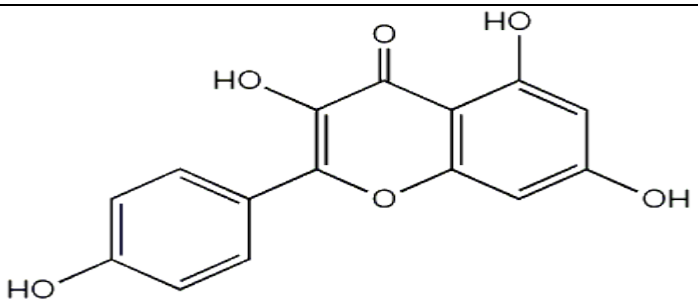
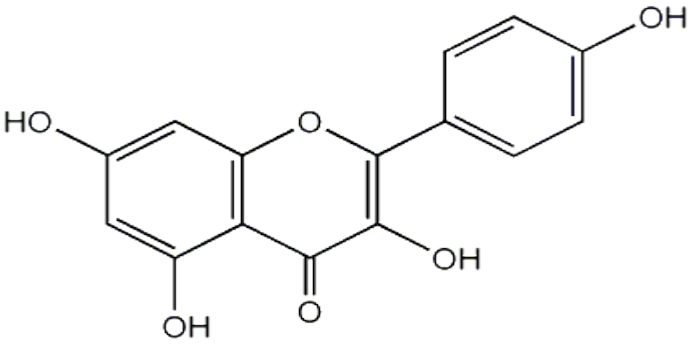
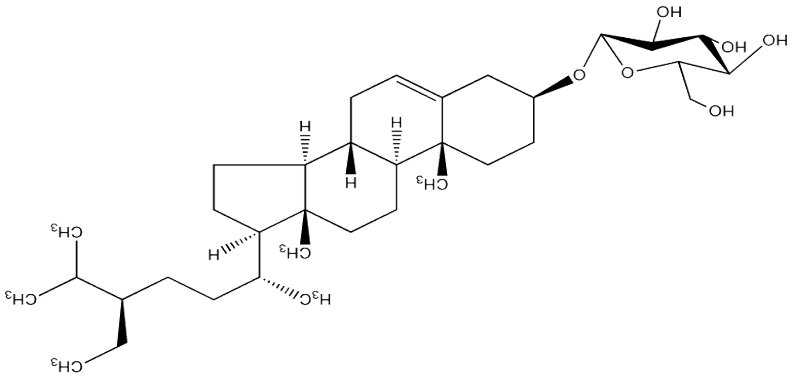
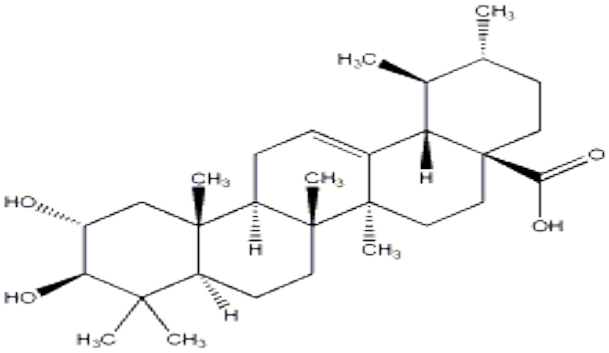
Table 1. Images of compounds from the plant *Centella asiatica* (Gotu kola), *Centella asiatica* plant

Nu	Coumpound	Chemical Structure

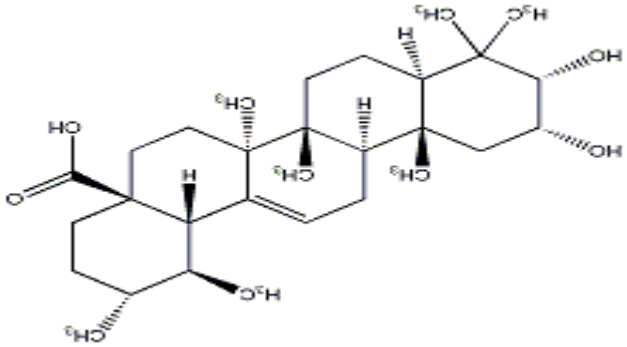
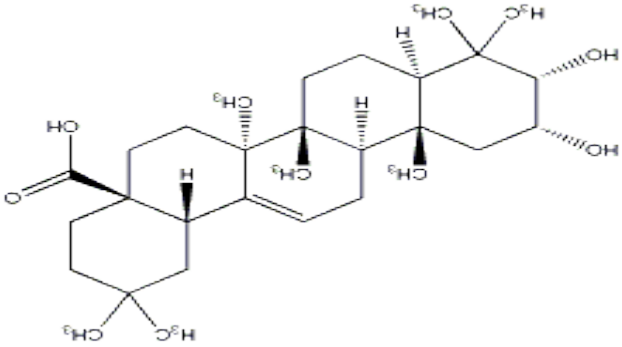
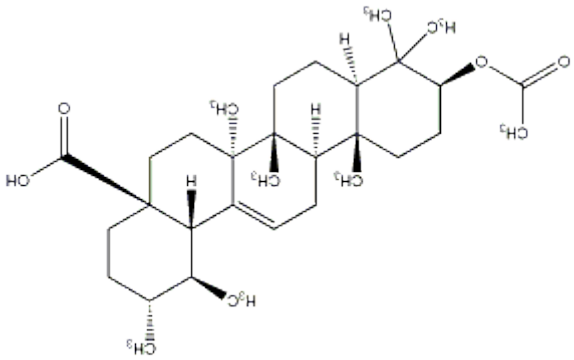
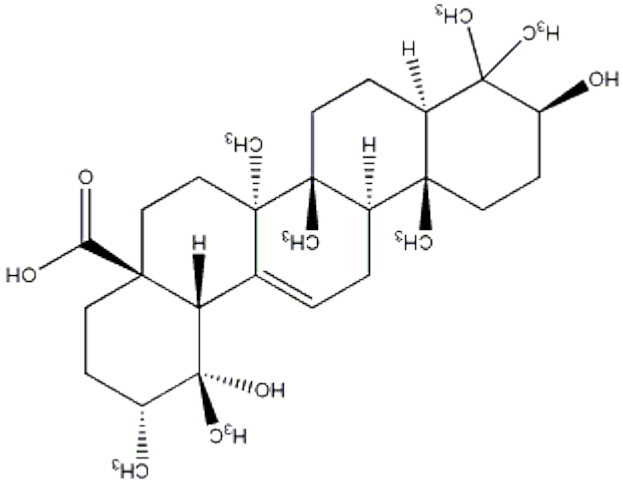
https://jurnal.rocewisdomaceh.com/index.php/roce e-ISSN : 3032-4505
Vol. 3, No. 2, Thn. 2026
https://doi.org/10.71275/roce.v3i2.212

Nu	Coumpound	Chemical Structure
1.	Labiatenic acid	
2.	beta-Caryophyllene	
3.	alpha-Caryophyllene (obsol.)	
4.	Asiatic acid	

https://jurnal.rocewisdomaceh.com/index.php/roce e-ISSN : 3032-4505
Vol. 3, No. 2, Thn. 2026
https://doi.org/10.71275/roce.v3i2.212

Nu	Coumpound	Chemical Structure
5.	Kaempferol	
6.	Quercetin	
7.	β-Sitosterol glucoside	
8.	2α,3β-Dihydroxyursolic acid	

Jurnal Pertanian Terapan of JURNAL ROCE (AGROSCIENCE)
https://jurnal.rocewisdomaceh.com/index.php/roce e-ISSN : 3032-4505
Vol. 3, No. 2, Thn. 2026
https://doi.org/10.71275/roce.v3i2.212

Nu	Coumpound	Chemical Structure
9.	2α,3α-Dihydroxyursolic acid	
10.	3-Epimaslinic acid	
11.	Acetylursolic acid	
12.	Pomolic acid	

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Vol. 3, No. 2, Thn. 2026
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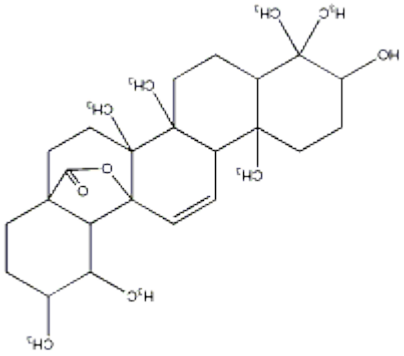
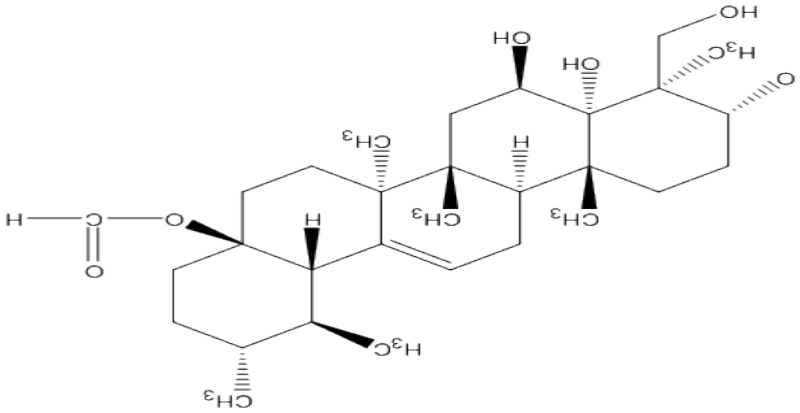
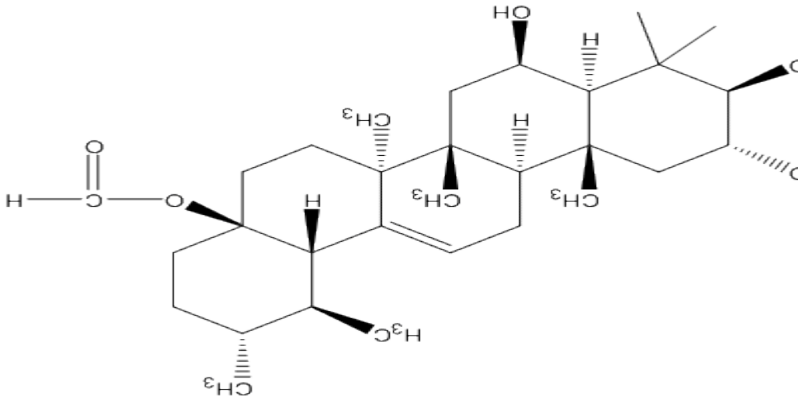
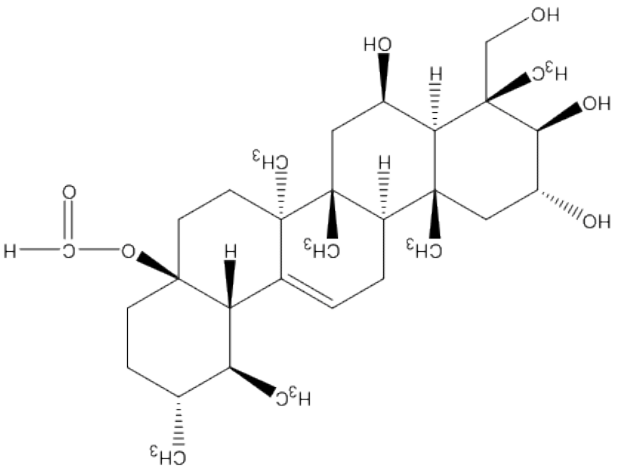
Nu	Coumpound	Chemical Structure
13.	Dehydroursolic acid lactone	
14.	Isothiocyanic acid	
15.	Madasiatic acid	
16.	Madecassic acid	

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Vol. 3, No. 2, Thn. 2026
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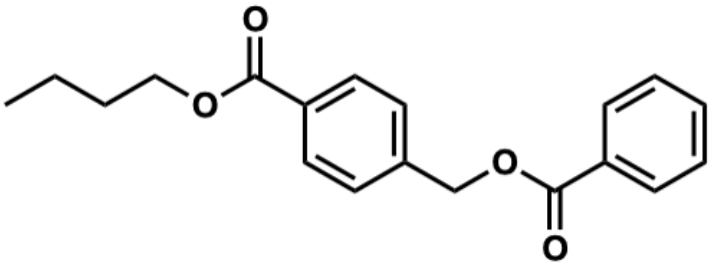
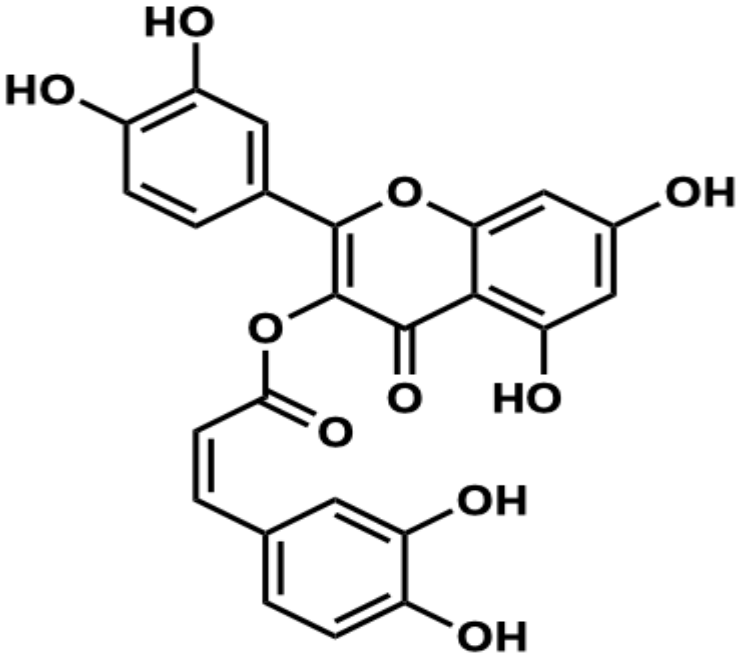
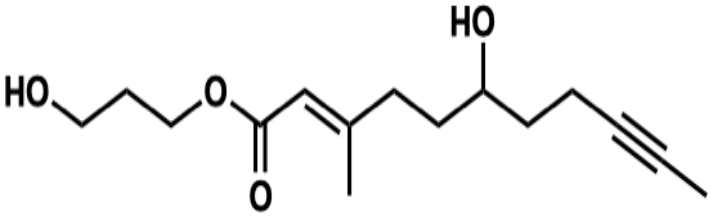
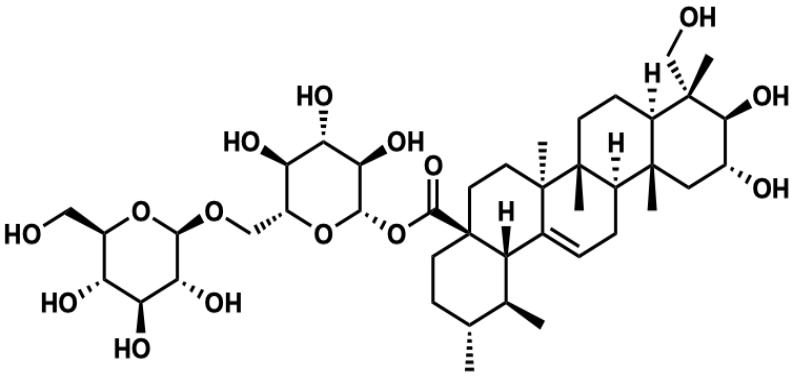
Nu	Coumpound	Chemical Structure
17.	Asiaticin	
18.	cis-Caffeoylquercetin	
19.	Centellicin	
20.	Asiaticoside E	

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Vol. 3, No. 2, Thn. 2026
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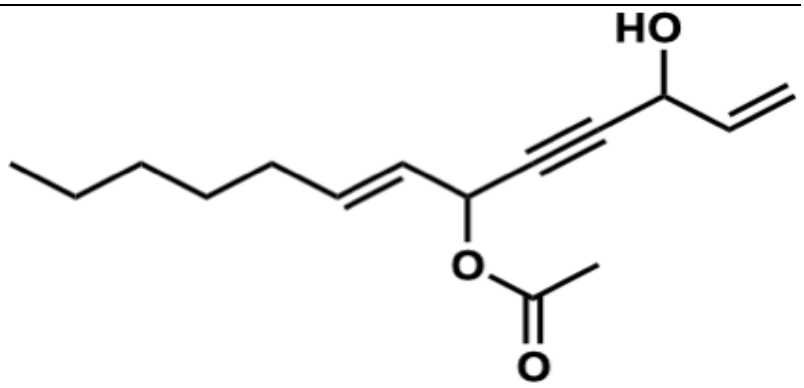
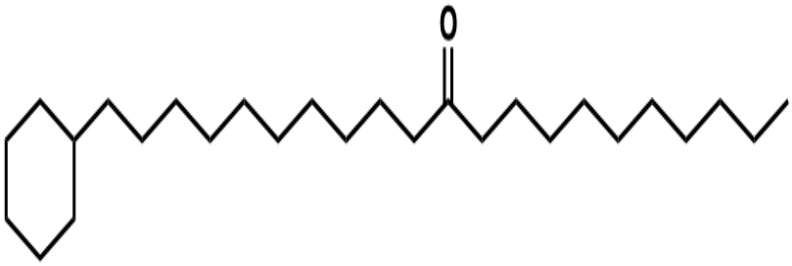
Nu	Coumpound	Chemical Structure
21.	Centellin	
22.	Cyclohexyl heneicosanone	

Table 2. SMILES code data of the Centella asiatica plant

Nu	Coumpound	SMILES
1.	Labiatenic acid	O=C(/C=C/c1ccc(O)c(O)c1)O[C@H](Cc1ccc(O)c(O)c1)C(=O)O
2.	beta-Caryophyllene	C=C1CC/C=C(C)CC[C@@H]2[C@@H]1CC2(C)C
3.	α-Caryophyllene	C/C1=CCC/C(C)=C/CC(C)(C)/C=C/C1
4.	Asiatic acid	C[C@H]1[C@H](C)CC[C@]2(C(=O)O)CC[C@]3(C)C(=CC[C@@H]4[C@@]5(C)C[C@@H](O)[C@H](O)[C@@](C)(CO)[C@@H]5CC[C@]43C)[C@H]12
5.	Kaempferol	O=c1c(O)c(-c2ccc(O)cc2)oc2cc(O)cc(O)c12
6.	Quercetin	O=c1c(O)c(-c2ccc(O)c(O)c2)oc2cc(O)cc(O)c12
7.	β-Sitosterol glucoside	CC[C@H](CC[C@@H](C)[C@H]1CC[C@H]2[C@@H]3CC=C4C[C@@H](O[C@@H]5OC(CO)[C@@H](O)[C@H](O)C5O)CC[C@]4(C)[C@H]3CC[C@]12C)C(C)C
8.	2α,3β-Dihydroxyursolic acid	C[C@H]1[C@H](C)CC[C@]2(C(=O)O)CC[C@]3(C)C(=CC[C@@H]4[C@@]5(C)C[C@@H](O)[C@H](O)C(C)(C)[C@@H]5CC[C@]43C)[C@H]12
9.	2α,3α-Dihydroxyursolic acid	C[C@H]1[C@H](C)CC[C@]2(C(=O)O)CC[C@]3(C)C(=CC[C@@H]4[C@@]5(C)C[C@@H](O)[C@@H](O)C(C)(C)[C@@H]5CC[C@]43C)[C@H]12
10.	3-Epimaslinic acid	CC1(C)CC[C@]2(C(=O)O)CC[C@]3(C)C(=CC[C@@H]4[C@@]5(C)C[C@@H](O)[C@@H](O)C(C)(C)[C@@H]5CC[C@]43C)[C@@H]2C1
11.	Acetylursolic acid	CC(=O)O[C@H]1CC[C@]2(C)[C@H]3CC=C4[C@@H]5[C@@H](C)[C@H](C)CC[C@]5(C(=O)O)CC[C@@]4(C)[C@]3(C)CC[C@H]2C1(C)C
12.	Pomolic acid	C[C@@H]1CC[C@]2(C(=O)O)CC[C@]3(C)C(=CC[C@@H]4[C@@]5(C)CC[C@H](O)C(C)(C)[C@@H]5CC[C@]43C)[C@@H]2[C@]1(C)O
13.	Dehydroursolic acid lactone	CC1CCC23CCC4(C)C5(C)CCC6C(C)(C)C(O)CCC6(C)C5C=CC4(OC2=O)C3C1C
14.	Isothiocyanic acid	C[C@H]1[C@H](C)CC[C@]2(OC=O)CC[C@]3(C)C(=CC[C@@H]4[C@@]5(C)CC[C@@H](O)[C@](C)(CO)[C@]5(O)[C@H](O)C[C@]43C)[C@H]12
15.	Madasiatic acid	C[C@H]1[C@H](C)CC[C@]2(OC=O)CC[C@]3(C)C(=CC[C@@H]4[C@@]5(C)C[C@

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https://jurnal.rocewisdomaceh.com/index.php/roce e-ISSN : 3032-4505
Vol. 3, No. 2, Thn. 2026
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		@H](O)[C@H](O)C(C)(C)[C@@H]5[C@H](O)C[C@]43C)[C@H]12
16.	Madecassic acid	C[C@H]1[C@H](C)CC[C@]2(OC=O)CC[C@]3(C)C(=CC[C@@H]4[C@@]5(C)C[C@@H](O)[C@H](O)[C@@](C)(CO)[C@@H]5[C@H](O)C[C@]43C)[C@H]12
17.	Asiaticin	CCCCOC(=O)c1ccc(COC(=O)c2ccccc2)cc1
18.	cis-Caffeoylquercetin	O=C(/C=Cc1ccc(O)c(O)c1)Oc1c(-c2ccc(O)c(O)c2)oc2cc(O)cc(O)c2c1=O
19.	Centellicin	CC#CCCC(O)CC/C(C)=C/C(=O)OCCCO
20.	cis-p-Coumaroylkaempferol	O=C(/C=C/c1ccc(O)cc1)Oc1c(-c2ccc(O)cc2)oc2cc(O)cc(O)c2c1=O
21.	Centellin	C=CC(O)C#CC(/C=C/CCCCC)OC(C)=O
22.	Cyclohexyl heneicosanone	CCCCCCCCCCC(=O)CCCCCCCCCCC1CCCCC1

Table 3. Antifungal data of the *Centella asiatica* plant based on analysis using PASS Online

Nu	Coumpound	Pa% anti-fungal
1.	Labiatenic acid	0.461
2.	beta-Caryophyllene	0.582
3.	α-Caryophyllene	0.339
4.	Asiatic acid	0.651
5.	Kaempferol	0.651
6.	Quercetin	0.49
7.	β-Sitosterol glucoside	0.722
8.	2α,3β-Dihydroxyursolic acid	0.623
9.	2α,3α-Dihydroxyursolic acid	0.623
10.	3-Epimaslinic acid	0.608
11.	Acetylursolic acid	0.624
12.	Pomolic acid	0.526
13.	Dehydroursolic acid lactone	0.52
14.	Isothiocyanic acid	0.309
15.	Madasiatic acid	0.285
16.	Madecassic acid	0.349
17.	Asiaticin	0.344
18.	cis-Caffeoylquercetin	0.634
19.	Centellicin	0.655
20.	cis-p-Coumaroylkaempferol	0.637
21.	Centellin	0.715
22.	Cyclohexyl heneicosanone	0.502

Table 4a. In Silico Data from SwissADME Supporting the Antifungal Activity of *Centella asiatica* for Controlling Fungi in Oil Palm Plants

Nu	Coumpound	Water Solubility		Lipophilicity (LogP)	Bioavailability score
		Log S (ESOL)	Class	Consensus Log $P_{o/w}$	
1.	Labiatenic acid	-1.95	Very soluble	-	0.56
2.	beta-Caryophyllene	-1.11	Very soluble	-	0.55
3.	α-Caryophyllene	-1.11	Very soluble	-	0.55
4.	Asiatic acid	-2.74	Very soluble	-	0.56

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Vol. 3, No. 2, Thn. 2026
https://doi.org/10.71275/roce.v3i2.212

Nu	Coumpound	Water Solubility		Lipophilicity (LogP)	Bioavailability score
		Log S (ESOL)	Class	Consensus Log $P_{o/w}$	
5.	Kaempferol	-2.11	Soluble	-	0.55
6.	Quercetin	-2.19	Soluble	-	0.55
7.	β-Sitosterol glucoside	-2.82	Soluble	-	0.55
8.	2α,3β-Dihydroxyursolic acid	-2.70	Soluble	-	0.56
9.	2α,3α-Dihydroxyursolic acid	-2.70	Soluble		0.56
10.	3-Epimaslinic acid	-2.70	Soluble	-	0.56
11.	Acetylursolic acid	-2.73	Soluble	-	0.85
12.	Pomolic acid	-2.70	Soluble	-	0.56
13.	Dehydroursolic acid lactone	-2.66	Soluble	-	0.55
14.	Isothiocyanic acid	-2.77	Soluble	-	0.55
15.	Madasiatic acid	-2.64	Soluble	-	0.55
16.	Madecassic acid	-2.77	Soluble	-	0.55
17.	Asiaticin	-1.57	Very soluble	-	0.55
18.	cis-Caffeoylquercetin	-2.87	Soluble	-	0.55
19.	Centellicin	-0.84	Very soluble	-	0.55
20.	cis-p-Coumaroylkaempferol	-2.70	Soluble	-	0.55
21.	Centellin	-0.86	Very soluble	-	0.55
22.	Cyclohexyl heneicosanone	-0.95	Very soluble	-	0.55

Table 4b. In Silico Drug-Likeness Data from SwissADME Supporting the Antifungal Activity of *Centella asiatica* for Controlling Fungi in Oil Palm Plants

No	Coumpound	Drug-likeness				
		Lipinski	Ghose	Veber	Egan	Muegge
1.	Labiatenic acid	Yes	Yes	No	No	Yes
2.	beta-Caryophyllene	Yes	Yes	Yes	Yes	No
3.	α-Caryophyllene	Yes	Yes	Yes	Yes	No
4.	Asiatic acid	Yes	No	Yes	Yes	Yes
5.	Kaempferol	Yes	Yes	Yes	Yes	Yes
6.	Quercetin	Yes	Yes	Yes	Yes	Yes
7.	β-Sitosterol glucoside	Yes	No	Yes	Yes	Yes
8.	2α,3β-Dihydroxyursolic acid	Yes	No	Yes	No	Yes
9.	2α,3α-Dihydroxyursolic acid	Yes	No	Yes	No	Yes
10.	3-Epimaslinic acid	Yes	No	Yes	No	Yes
11.	Acetylursolic acid	Yes	No	Yes	No	Yes
12.	Pomolic acid	Yes	No	Yes	No	Yes
13.	Dehydroursolic acid lactone	Yes	No	Yes	No	Yes
14.	Isothiocyanic acid	Yes	No	Yes	Yes	Yes
15.	Madasiatic acid	Yes	No	Yes	Yes	Yes
16.	Madecassic acid	Yes	No	Yes	Yes	Yes
17.	Asiaticin	Yes	Yes	Yes	Yes	Yes

No	Coumpound	Drug-likeness				
		Lipinski	Ghose	Veber	Egan	Muegge
18.	cis-Caffeoylquercetin	Yes	No	No	No	No
19.	Centellicin	Yes	Yes	Yes	Yes	Yes
20.	cis-p-Coumaroylkaempferol	Yes	Yes	Yes	No	Yes
21.	Centellin	yes	yes	yes	yes	yes
22.	Cyclohexyl heneicosanone	yes	no	no	no	no

Table 4c. In Silico Physicochemical Properties Data from SwissADME Supporting the Antifungal Activity of *Centella asiatica* for Controlling Fungi in Oil Palm Plants

Nu	Compound	Physicochemical Properties								
		Mol. Weight (g/mol)	Number of. heavy atoms	Num. arom heavy atoms	Fraction Csp3	Num. rotatable bonds	Num. H-bond acceptors	Num. H-bond donors	Molar refractivity	TPSA (Å²)
1.	Labiatenic acid	360.31	26	12	0.11	7	8	5	91.40	144.52
2.	beta-Caryophyllene	204.35	15	0	0.73	0	0	0	68.78	0.00
3.	α-Caryophyllene	204.35	15	0	0.60	0	0	0	70.42	0.00
4.	Asiatic acid	488.70	35	0	0.90	2	5	4	139.24	97.99
5.	Kaempferol	286.24	21	16	0.00	1	6	4	76.01	111.13
6.	Quercetin	302.24	22	16	0.00	1	7	5	78.04	131.36
7.	β-Sitosterol glucoside	576.85	41	0	0.94	9	6	4	165.61	99.38
8.	2α,3β-Dihydroxyursolic acid	472.70	34	0	0.90	1	4	3	138.08	77.76
9.	2α,3α-Dihydroxyursolic acid	472.70	34	0	0.90	1	4	3	138.08	77.76
10.	3-Epimaslinic acid	472.70	34	0	0.90	1	4	3	137.82	77.76
11.	Acetylursolic acid	498.74	36	0	0.88	3	4	1	146.65	63.60
12.	Pomolic acid	472.70	34	0	0.90	1	4	3	138.11	77.76
13.	Dehydroursolic acid lactone	454.68	33	0	0.90	0	3	1	134.35	46.53
14.	Isothiocyanic acid	504.70	36	0	0.90	3	6	4	140.64	107.22
15.	Madasiatic acid	473.66	34	0	0.90	2	5	3	133.57	86.99

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Vol. 3, No. 2, Thn. 2026
https://doi.org/10.71275/roce.v3i2.212

Nu	Compound	Physicochemical Properties								
		Mol. Weight (g/mol)	Number of. heavy atoms	Num. arom heavy atoms	Fraction Csp3	Num. rotatable bonds	Num. H-bond acceptors	Num. H-bond donors	Molar refractivity	TPSA (Å²)
16.	Madecassic acid	504.70	36	0	0.90	3	6	4	140.60	107.22
17.	Asiaticin	312.36	23	12	0.26	9	4	0	87.91	52.60
18.	cis-Caffeoylquercetin	464.38	34	22	0.00	5	10	6	121.17	177.89
19.	Centellicin	268.35	19	0	0.67	10	4	2	75.52	66.76
20.	cis-p-Coumaroylkaempferol	432.38	32	22	0.00	5	8	4	117.12	137.43
21.	Centellin	250.33	18	0	0.53	8	3	1	73.88	46.53
22.	Cyclohexylheneicosanone	392.70	28	0	0.96	20	1	0	129.99	17.07

Table 5. In Silico Data of *Centella asiatica* from PKCSM

Nu	Nama Senyawa	AMES Toxicity	Hepatotoxcity	Environmental Toxicity	
				T. pyriformis toxicity (log ug/L)	Minnow toxicity (log Mm)
1.	Labiatenic acid	No	No	0.285	1.375
2.	beta-Caryophyllene	No	No	1.409	0.413
3.	α-Caryophyllene	No	No	1.451	0.716
4.	Asiatic acid	No	No	0.285	0.311
5.	Kaempferol	Yes	No	0.312	1.082
6.	Quercetin	No	No	0.293	1.328
7.	β-Sitosterol glucoside	No	No	0.285	0.823
8.	2α,3β-Dihydroxyursolic acid	No	No	0.286	-0.284
9.	2α,3α-Dihydroxyursolic acid	No	No	0.286	-0.284
10.	3-Epimaslinic acid	No	No	0.286	-0.069
11.	Acetylursolic acid	No	No	0.286	-3.297
12.	Pomolic acid	No	No	0.297	0.373
13.	Dehydroursolic acid lactone	No	No	0.362	-0.633
14.	Isothiocyanic acid	No	No	0.285	0.872
15.	Madasiatic acid	No	No	0.297	0.403
16.	Madecassic acid	No	No	0.285	1.138
17.	Asiaticin	No	No	0.51	-1.437
18.	cis-Caffeoylquercetin	No	No	0.285	0.488
19.	Centellicin	Yes	No	1.209	1.497
20.	cis-p-Coumaroylkaempferol	No	No	0.285	8.671
21.	Centellin	Yes	No	1.649	1.176

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Vol. 3, No. 2, Thn. 2026
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Nu	Nama Senyawa	AMES Toxicity	Hepatotoxcity	Environmental Toxicity	
				T. pyriformis toxicity (log ug/L)	Minnow toxicity (log Mm)
22.	Cyclohexyl heneicosanone	No	No	0.788	-1.105

Based on PASS Online analysis, the active compounds of Centella asiatica exhibited diverse antifungal activity, with most compounds showing Pa values > 0.5, indicating promising antifungal potential. The highest activities were observed for 3-O-beta-D-Glucopyranosyl sitosterol (0.722), Centellin (0.715), Centellicin (0.655), Asiatic acid (0.651), and Kaempferol (0.651), suggesting that triterpenoids and flavonoids are the principal antifungal constituents of pegagan. Compounds with Pa values between 0.3 and 0.5, such as quercetin and several ursolic acid derivatives, still exhibit potential biological activity. Triterpenoids, including asiatic acid, madecassic acid, acetylursolic acid, and pomolic acid, exert antifungal effects by disrupting fungal membranes through interaction with ergosterol. In contrast, flavonoids inhibit cell wall synthesis, interfere with energy metabolism, and suppress spore formation. Sesquiterpenes such as β-caryophyllene also contribute through membrane disruption, although with lower activity than triterpenoids. Overall, these findings indicate that pegagan is a promising source of environmentally friendly natural biofungicides (Olszowy-Tomczyk *et al*., 2022; Khwaza & Aderibigbe, 2024; Wang *et al*., 2022; Yanthi *et al*., 2022).

SwissADME drug-likeness analysis showed that nearly all compounds satisfied Lipinski's rule, indicating favorable molecular properties for biological activity (de Aguiar Mello & Gonçalves, 2026). Kaempferol, quercetin, asiaticin, centellin, and centellicin met all major drug-likeness criteria, reflecting balanced molecular size, polarity, flexibility, and lipophilicity, which support antifungal activity (Singh & Singh, 2024). Most triterpenoids complied with the Lipinski, Veber, and Muegge rules, but showed limited compliance with the Ghose and Egan rules due to their larger molecular size. Nevertheless, these properties favor interaction with fungal lipid membranes and inhibition of ergosterol biosynthesis (Yanthi *et al*., 2022). Sesquiterpenes such as β-caryophyllene also exhibited good drug-likeness profiles, supporting their development as sustainable botanical fungicides (Lawan & Mustapha, 2026).

Analysis of physicochemical properties indicated that most compounds possess molecular characteristics favorable for antifungal activity. Triterpenoids exhibited suitable molecular weight and high fraction Csp3, supporting structural stability and affinity toward fungal targets (Odhiambo *et al*., 2025). Most compounds had TPSA values below 140 Å², indicating good membrane permeability, whereas compounds with higher TPSA may exhibit lower permeability but stronger interactions with fungal proteins (Yang *et al*., 2025). Flavonoids such as kaempferol and quercetin showed high hydrogen-bonding capacity, enhancing inhibition of fungal enzymes and cell wall synthesis (Kumar & Pandey, 2013). In contrast, sesquiterpenes such as β-caryophyllene are highly hydrophobic, facilitating rapid penetration into fungal membranes and contributing to membrane disruption and inhibition of mycelial growth (Khan *et al*., 2023).

The pkCSM analysis demonstrated that most active compounds possess favorable safety profiles, with nearly all predicted to be non-mutagenic and non-hepatotoxic, supporting their development as environmentally friendly biofungicides (Deresa & Diriba, 2023). Although kaempferol, centellin, and centellicin were predicted to be mutagenic, these findings require confirmation through in vitro and in vivo studies, whereas hepatotoxicity was not predicted for any compound (Chauhan *et al*., 2026). Environmental toxicity analysis showed generally low toxicity to aquatic organisms, particularly for triterpenoids such as asiatic acid, pomolic acid, and madecassic acid, although several compounds require dose optimization due to relatively higher toxicity values. Overall, the pkCSM results support the potential of Centella asiatica as a safe, sustainable, and environmentally friendly source of natural antifungal agents for controlling fungal diseases in oil palm plants (Shaizee *et al*., 2025; Kudadiri, 2023).

CONCLUSION

Based on in silico analyses using PASS Online, SwissADME, and pkCSM, the active compounds of Centella asiatica demonstrated good antifungal potential, supported by favorable pharmacokinetic characteristics, drug-likeness, physicochemical properties, and relatively low toxicity. These results indicate that pegagan has strong potential to be developed as an environmentally friendly natural biofungicide for controlling fungal diseases in oil palm plants.

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