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.v3i2.208

IN SILICO ANALYSIS OF ANTIFUNGAL POTENTIAL AND PHARMACOKINETIC CHARACTERISTICS OF SHALLOT (*Allium cepa* L.) SECONDARY METABOLITES USING PASS ONLINE AND SWISSADME

ANALISIS IN SILICO POTENSI ANTIFUNGI DAN KARAKTERISTIK FARMAKOKINETIK METABOLIT SEKUNDER BAWANG MERAH (*Allium cepa* L.) MENGGUNAKAN PASS ONLINE DAN SWISSADME

Erwandi [1*], Rahadatul Aisy Wafadhianti Indrapaslah[1], Ahdilan Juliansyah[1], Hikmal[1], Juliadi Nur Rahim[1], Dodi Iskandar[2]

[1] Plantation Crop Cultivation Study Program, Agricultural Technology Department, Pontianak State Polytechnic
[2] Integrated Plantation Product Processing Study Program, Agricultural Technology Department, Pontianak State Polytechnic

* Correspondent Email: dilanjuliansyah49@gmail.com

Abstract

Shallot (*Allium cepa* L.) contains various secondary metabolites with potential biological activities, including antifungal activity. This study aimed to evaluate the antifungal potential and pharmacokinetic characteristics of secondary metabolites from shallot using *in silico* approaches with PASS Online and SwissADME. PASS Online analysis demonstrated that all identified compounds possessed potential antifungal activity with varying Probability of Activity (Pa) values. Among the compounds, (+)-Dihydroeleutherinol showed the highest antifungal potential with a Pa value of 0.608, followed by (-)-3-[2-(Acetyloxy)propyl]-2-hydroxy-8-methoxy-1,4-naphthoquinone and (-)-Hongconin with Pa values of 0.599 and 0.594, respectively. The antifungal activity of these compounds is associated with their ability to disrupt fungal cell membranes, inhibit cell wall synthesis, and induce oxidative stress via the formation of reactive oxygen species (ROS). SwissADME analysis indicated that all compounds exhibited favorable pharmacokinetic and physicochemical profiles, including high water solubility, balanced lipophilicity, and acceptable bioavailability scores ranging from 0.55 to 0.56. Drug-likeness analysis further revealed that all compounds complied with Lipinski, Ghose, Veber, Egan, and Muegge rules, indicating good oral absorption potential and membrane permeability. In addition, physicochemical property analysis showed that all compounds had molecular weights below 500 g/mol, low topological polar surface area (TPSA), balanced hydrogen-bonding properties, and moderate molecular flexibility, which are important characteristics for drug development. Compounds such as (+)-Eleutherin, (-)-Isoeleutherin, and (+)-Dihydroeleutherinol demonstrated particularly promising profiles due to their balanced physicochemical and pharmacokinetic properties. Overall, the combined PASS Online and SwissADME analyses suggest that shallot secondary metabolites have strong potential as natural antifungal agents. However, further *in vitro* and *in vivo* studies are required to validate their biological activity, safety, toxicity, and mechanisms of action against pathogenic fungi.

Keywords: *Shallot, Allium cepa L., antifungal activity, secondary metabolites, PASS Online, SwissADME, drug-likeness.*

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.v3i2.208

Abstrak

Bawang merah (*Allium cepa* L.) dikenal sebagai sumber kaya metabolit sekunder dengan berbagai aktivitas biologis, termasuk potensi antijamur. Penelitian ini bertujuan untuk mengevaluasi potensi antijamur serta sifat farmakokinetik metabolit sekunder bawang merah menggunakan pendekatan *in silico* melalui analisis PASS Online dan SwissADME. Prediksi PASS Online menunjukkan bahwa seluruh senyawa yang diuji memiliki potensi aktivitas antijamur dengan nilai Probability of Activity (Pa) yang bervariasi. Di antara senyawa tersebut, (+)-Dihydroeleutherinol menunjukkan potensi antijamur tertinggi (Pa = 0,608), diikuti oleh (-)-3-[2-(Acetyloxy)propyl]-2-hydroxy-8-methoxy-1,4-naphthoquinone (Pa = 0,599) dan (-)-Hongconin (Pa = 0,594). Mekanisme aktivitas antijamur yang diprediksi dari senyawa-senyawa tersebut berkaitan dengan gangguan membran sel jamur, penghambatan sintesis dinding sel, serta induksi stres oksidatif melalui pembentukan reactive oxygen species (ROS). Analisis SwissADME menunjukkan bahwa seluruh senyawa memiliki profil farmakokinetik dan sifat fisikokimia yang baik, termasuk kelarutan air yang baik, lipofilisitas yang seimbang, serta skor bioavailabilitas yang dapat diterima berkisar antara 0,55–0,56. Evaluasi drug-likeness menunjukkan bahwa semua senyawa memenuhi berbagai aturan penyaringan seperti Lipinski, Ghose, Veber, Egan, dan Muegge, yang mengindikasikan potensi absorpsi oral dan permeabilitas membran yang baik. Selain itu, analisis sifat fisikokimia menunjukkan bahwa seluruh senyawa memiliki berat molekul di bawah 500 g/mol, nilai topological polar surface area (TPSA) yang rendah, kemampuan ikatan hidrogen yang memadai, serta fleksibilitas molekul yang moderat—yang merupakan karakteristik penting dalam pengembangan obat. Secara khusus, (+)-Eleutherin, (-)-Isoeleutherin, dan (+)-Dihydroeleutherinol menunjukkan profil yang paling menjanjikan karena memiliki keseimbangan sifat fisikokimia dan farmakokinetik yang baik. Secara keseluruhan, analisis terpadu PASS Online dan SwissADME menunjukkan bahwa metabolit sekunder bawang merah memiliki potensi yang kuat sebagai kandidat obat antijamur alami. Namun, diperlukan penelitian lanjutan melalui uji *in vitro* dan *in vivo* untuk mengonfirmasi aktivitas biologis, profil keamanan, toksisitas, serta mekanisme kerjanya terhadap jamur patogen.

Kata Kunci: Bawang merah, *Allium cepa* L, aktivitas antijamur, metabolit sekunder, PASS Online, SwissADME, drug-likeness

INTRODUCTION

Fungal infections remain a major global health concern due to the increasing incidence of fungal diseases and the growing resistance of pathogenic fungi to conventional antifungal drugs. Fungal pathogens can infect humans, animals, and plants, causing serious health complications and economic losses. In humans, fungal infections can range from mild superficial infections to severe invasive diseases, particularly among immunocompromised patients. The emergence of antifungal resistance has encouraged scientists to search for alternative antifungal agents derived from natural products (van Rhijn & Rhodes, 2025). Medicinal plants are widely recognized as valuable sources of bioactive compounds, containing diverse secondary metabolites with antibacterial, antioxidant, anti-inflammatory, antiviral, and antifungal activities.

One medicinal plant that has gained increasing scientific interest is shallot (*Allium cepa* L.). Shallot is commonly cultivated and consumed as both a culinary spice and a traditional herbal remedy in many countries, including Indonesia. Besides their nutritional importance, shallots contain various phytochemicals that contribute to their therapeutic properties. Previous studies have shown that shallots contain flavonoids, alkaloids, tannins, saponins, phenolic compounds, and naphthoquinones that exhibit significant antimicrobial and antifungal activities

(Prabawati *et al*., 2026). Traditionally, shallots have been used to treat infections, inflammation, fever, and digestive disorders. The increasing demand for plant-based medicines has stimulated further research into the pharmacological potential of shallot secondary metabolites as natural antifungal agents.

Among the bioactive compounds identified in shallot, naphthoquinone derivatives such as eleutherin, isoeleutherin, eleutherinol, and hongconin are considered major contributors to antifungal activity. Naphthoquinone compounds possess broad-spectrum antimicrobial properties because they can disrupt fungal cell membrane integrity, interfere with mitochondrial respiration, and induce oxidative stress through the production of reactive oxygen species (ROS) (Chen *et al.*, 2026). These mechanisms may lead to fungal cell damage and death. Furthermore, quinone derivatives can inhibit ergosterol biosynthesis, which is essential for maintaining fungal membrane stability and permeability (Sharma *et al*., 2026). Due to these mechanisms, quinone-based compounds are increasingly considered promising candidates for developing natural antifungal drugs.

The discovery and development of antifungal agents from natural products requires a comprehensive evaluation of biological activity, toxicity, pharmacokinetics, and physicochemical properties. Conventional laboratory screening methods are often expensive, time-consuming, and labor-intensive. Therefore, computational approaches such as *in silico* analysis have become increasingly important in the early stages of drug discovery (Sadybekov & Katritch, 2023). *In silico* methods enable researchers to rapidly and efficiently predict biological activity, pharmacokinetic behavior, and drug-likeness profiles before conducting experimental studies. These computational approaches can significantly reduce research costs and improve the identification of promising bioactive compounds (Oyejide *et al*., 2025).

One widely used computational tool for predicting biological activity is PASS Online (Prediction of Activity Spectra for Substances). PASS Online estimates the probability of compounds exhibiting specific biological activities based on their chemical structures. The prediction results are expressed as Probability of Activity (Pa) values, where higher Pa values indicate greater probabilities of biological activity (Pogodin *et al*., 2018). PASS Online has been extensively applied in natural product screening because it provides rapid and reliable predictions of pharmacological potential. Compounds with Pa values above 0.5 are generally considered to possess promising biological activities and are suitable for further evaluation through *in vitro* and *in vivo* studies (Ibrahim & Rizk, 2021).

In addition to biological activity prediction, pharmacokinetic and physicochemical evaluations are essential for determining the suitability of compounds as drug candidates. SwissADME is a popular web-based platform used to evaluate absorption, distribution, metabolism, excretion, and drug-likeness properties of chemical compounds (Daina et al., 2020). Parameters such as molecular weight, lipophilicity, water solubility, topological polar surface area (TPSA), hydrogen-bonding capacity, and bioavailability score are critical for predicting membrane permeability and oral absorption. Drug-likeness analysis based on Lipinski, Ghose, Veber, Egan, and Muegge rules is also important in evaluating whether compounds possess favorable physicochemical characteristics for drug development (Miebs *et al*., 2024). Compounds

https://jurnal.rocewisdomaceh.com/index.php/roce e-ISSN : 3032-4505
Vol. 3, No. 2, Thn. 2026
https://doi.org/10.71275/roce.v3i2.208

that satisfy these criteria generally demonstrate improved pharmacokinetic profiles and greater probabilities of success in drug development.

Several recent studies have highlighted the effectiveness of integrating PASS Online and SwissADME analyses in identifying promising natural bioactive compounds. This combined *in silico* strategy enables simultaneous evaluation of biological activity and pharmacokinetic feasibility, thereby improving the selection of potential drug candidates (Ayoobi & Choi, 2026). Despite increasing interest in shallot metabolites, studies focusing specifically on the antifungal potential and pharmacokinetic properties of naphthoquinone compounds from shallot remain limited. Therefore, further investigation is necessary to better understand the therapeutic potential of these compounds as natural antifungal agents.

Based on these considerations, this study aimed to evaluate the antifungal activity, physicochemical characteristics, pharmacokinetic properties, and drug-likeness profiles of secondary metabolites from shallot using PASS Online and SwissADME analyses. The findings of this study are expected to provide scientific evidence regarding the potential use of shallot metabolites as natural antifungal agents and contribute to the development of plant-based antifungal drugs in the future.

RESEARCH METHODS

This study used an *in silico* approach to evaluate the antifungal potential and pharmacokinetic properties of secondary metabolites from shallot (*Allium cepa* L.). The research consisted of several stages, including compound identification, prediction of antifungal activity, and analysis of pharmacokinetic, physicochemical, and drug-likeness properties using bioinformatics-based web tools. The *in silico* method is widely used in natural product research because it is efficient, cost-effective, and can predict the biological activity of compounds before laboratory testing (Aarón *et al*., 2025). In recent years, computational approaches have become increasingly important in accelerating natural product-based drug discovery and reducing experimental costs (Wang *et al*., 2026). Bioinformatics-based screening methods are also considered effective for identifying compounds with promising pharmacological properties and favorable pharmacokinetic profiles (Zhang *et al*., 2025). Furthermore, *in silico* analyses can provide preliminary information regarding compound absorption, distribution, metabolism, excretion, and toxicity, thereby supporting the early stages of drug development (Roney & Mohd Aluwi, 2024). The integration of PASS Online and SwissADME analyses has been widely used in recent studies to predict biological activity and assess the drug-likeness of bioactive plant metabolites (Daina *et al*., 2017).

RESULTS AND DISCUSSION

Table 1. SMILES Code Data of Shallot Plants

Nu	Compound	SMILES
1	(+)-Eleutherin	COc1cccc2c1C(=O)C1=C(C[C@H](C)O[C@@H]1C)C2=O

https://jurnal.rocewisdomaceh.com/index.php/roce e-ISSN : 3032-4505
Vol. 3, No. 2, Thn. 2026
https://doi.org/10.71275/roce.v3i2.208

Nu	Compound	SMILES
2	(-)-3-[2-(Acetyloxy)propyl]-2-hydroxy-8-methoxy-1,4-naphthoquinone	COc1cccc2c1C(=O)C(O)=C(C[C@@H](C)OC(C)=O)C2=O
3	(-)-Hongconin	COc1cccc2c(O)c3c(c(O)c12)[C@@H](C)O[C@H](C)C3=O
4	(-)-Isoeleutherin	COc1cccc2c1C(=O)C1=C(C[C@@H](C)O[C@@H]1C)C2=O
5	(+)-Dihydroeleutherinol	Cc1cc2cc(O)cc(O)c2c2c1C(=O)C[C@@H](C)O2
6	1,5-Dihydroxy-3-methylanthraquinone Ziganein	Cc1cc(O)c2c(c1)C(=O)c1c(O)cccc1C2=O
7	Eleutherinol	Cc1cc(=O)c2c(C)cc3cc(O)cc(O)c3c2o1

Table 2. Antifungal Data of Shallot Plants Based on Analysis Using PASS Online

Nu	Compound	Antifungal (Percentage of Activity Probability)
1	(+)-Eleutherin	0,583
2	(-)-3-[2-(Acetyloxy)propyl]-2-hydroxy-8-methoxy-1,4-naphthoquinone	0,599
3	(-)-Hongconin	0,594
4	(-)-Isoeleutherin	0,583
5	(+)-Dihydroeleutherinol	0,608
6	1,5-Dihydroxy-3-methylanthraquinone Ziganein	0,457
7	Eleutherinol	0,497

Table 3a. In Silico Data from SwissADME Supporting the Antifungal Activity of Shallot Plants

No	Compound	Water Solubility		Lipophilicity (LogP)	Bioavailability score
		Log *S* (ESOL)	Class	Consensus Log $P_{o/w}$	
1.	(+)-Eleutherin	-3.75	Very soluble	0.965	0.55
2.	(-)-3-[2-(Acetyloxy)propyl]-2-hydroxy-8-methoxy-1,4-naphthoquinone	-3.101	Very soluble	1.365	0.56
3.	(-)-Hongconin	-2.78	Very soluble	-3.57	0.55
4.	(-)-Isoeleutherin	-4.093	Very soluble	1.303	0.55
5.	(+)-Dihydroeleutherinol	2.987	Very soluble	-4.131	0.55
6.	1,5-Dihydroxy-3-methylanthraquinone Ziganein	-6.187	Very soluble	3.873	0.55
7.	Eleutherinol	-4.208	Very soluble	2.56	0.55

https://jurnal.rocewisdomaceh.com/index.php/roce e-ISSN : 3032-4505
Vol. 3, No. 2, Thn. 2026
https://doi.org/10.71275/roce.v3i2.208

Table 3b. In Silico Drug-Likeness Data from SwissADME Supporting the Antifungal Activity of Shallot Plants

Nu	Compound	Drug-likeness				
		Lipinski	Ghose	Veber	Egan	Muegge
1.	(+)-Eleutherin	Yes	Yes	Yes	Yes	Yes
2.	(-)-3-[2-(Acetyloxy)propyl]-2-hydroxy-8-methoxy-1,4-naphthoquinone	Yes	Yes	Yes	Yes	Yes
3.	(-)-Hongconin	Yes	Yes	Yes	Yes	Yes
4.	(-)-Isoeleutherin	Yes	Yes	Yes	Yes	Yes
5.	(+)-Dihydroeleutherinol	Yes	Yes	Yes	Yes	Yes
6.	1,5-Dihydroxy-3-methylanthraquinone Ziganein	Yes	Yes	Yes	Yes	Yes
7.	Eleutherinol	Yes	Yes	Yes	Yes	Yes

Table 3c. In Silico Physicochemical Properties Data from SwissADME Supporting the Antifungal Activity of Shallot Plants

Nu	Compound	Physicochemical Properties								
	Compound	Mol. weight	Number of. heavy atoms	Num. arom. heavy atoms	Fraction Csp3	Num. rotatable bonds	Num. H-bond acceptors	Num. H-bond donors	Molar Refractivity	TPSA (A^2)
1.	(+)-Eleutherin	272.30 g/mol	20	6	0.38	1	4	0	73.74	52.60 Å²
2.	(-)-3-[2-(Acetyloxy)propyl]-2-hydroxy-8-methoxy-1,4-naphthoquinone	304.29 g/mol	22	6	0.31	5	6	1	77.63	89.90 Å²
3.	(-)-Hongconin	288.30 g/mol	21	10	0.31	1	5	2	78.23	75.99 Å²
4.	(-)-Isoeleutherin	272.30 g/mol	20	6	0.38	1	4	0	73.74	52.60 Å²
5.	19	258.27 g/mol	19	10	0.27	0	4	2	72.34	66.76 Å²
6.	1,5-Dihydroxy-3-methylanthraquinone Ziganein	254.24 g/mol	19	12	0.07	0	4	2	68.76	74.60 Å²
7.	Eleutherinol	256.25 g/mol	19	14	0.13	0	4	2	73.97	70.67 Å²

Table 4. In Silico Data of Shallot Plants from PKCSM

No	Compound	AMES Toxicity	Hepatotoxicity	Environmental Toxicity	
				T.Pyriformis toxicity (log ug/L)	Minnow toxicity (log mM)
1.	(+)-Eleutherin	Yes	No	1.068	1.164
2.	(-)-3-[2-(Acetyloxy)propyl]-2-hydroxy-8-methoxy-1,4-naphthoquinone	No	No	0.671	2.07

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.v3i2.208

No	Compound	AMES Toxicity	Hepatotoxicity	Environmental Toxicity	
				T.Pyriformis toxicity (log ug/L)	Minnow toxicity (log mM)
3.	(-)-Hongconin	Yes	No	0.566	1.165
4.	(-)-Isoeleutherin	Yes	No	1.068	1.164
5.	(+)-Dihydroeleutherinol	Yes	No	0.915	1.069
6.	1,5-Dihydroxy-3-methylanthraquinone Ziganein	Yes	No	0.634	1.01
7.	Eleutherinol	Yes	No	0.407	0.913

The results of the analysis using PASS Online in Table 2 indicate that all compounds found in shallot plants exhibit potential antifungal activity with varying Probability of Activity (Pa) values. The p-value is used to assess the likelihood that a compound exhibits a specific biological activity. The higher the Pa value, the greater the probability that the compound possesses biological antifungal activity. Generally, a Pa value > 0.5 indicates sufficiently good activity potential and is considered worthy of further investigation through laboratory testing (both in vitro and in vivo) (Althubaiti, 2023). The compound with the highest activity value was (+)-Dihydroeleutherinol, with a Pa value of 0.608. This value indicates that the compound has the highest probability of being an antifungal agent compared with the other compounds. The antifungal activity of naphthoquinone and anthraquinone compounds is generally associated with their ability to disrupt fungal cell membrane integrity, inhibit cell wall synthesis, and induce oxidative stress through the formation of reactive oxygen species (ROS) (Chen *et al*., 2026). Therefore, the presence of the quinone structure in (+)-Dihydroeleutherinol is believed to play an important role in enhancing its biological activity.

The compounds (-)-3-[2-(Acetyloxy)propyl]-2-hydroxy-8-methoxy-1,4-naphthoquinone and (-)-Hongconin also showed high Pa values of 0.599 and 0.594, respectively. Both compounds are naphthoquinones known to possess broad antimicrobial activity, including against pathogenic fungi. Naphthoquinones can inhibit fungal growth by impairing mitochondrial function and disrupting electron transfer in microbial cells (Borba-Santos *et al*., 2022). This activity makes quinone derivative compounds promising candidates for the development of natural antifungal drugs. Meanwhile, the compounds (+)-Eleutherin and (-)-Isoeleutherin had Pa values of 0.583, indicating fairly good antifungal activity. Eleutherin is a secondary metabolite belonging to the naphthoquinone group commonly found in plants of the *Eleutherine* genus. This compound is known to exhibit various pharmacological activities, including antibacterial, antioxidant, and antifungal effects. The antifungal mechanism of eleutherin is thought to involve inhibition of ergosterol biosynthesis in fungal cell membranes, leading to disrupted membrane permeability and eventual cell death (Tanwar *et al*., 2024).

In contrast to the other compounds, Ziganein and Eleutherinol had Pa values below 0.5, namely 0.457 and 0.497, respectively. These values indicate that the antifungal potential of both

https://jurnal.rocewisdomaceh.com/index.php/roce e-ISSN : 3032-4505
Vol. 3, No. 2, Thn. 2026
https://doi.org/10.71275/roce.v3i2.208

compounds is relatively lower than that of the other compounds listed in the table. Nevertheless, these values still suggest the possibility of biological activity, meaning that both compounds may still be considered as supporting compounds or combined with other compounds to produce synergistic effects. Recent studies have shown that combinations of several plant secondary metabolites can enhance antifungal effectiveness through complementary mechanisms of action (Elhamouly *et al*., 2022).

Overall, the PASS Online analysis results demonstrate that secondary metabolite compounds in shallots have potential as natural antifungal agents. Compounds with the highest Pa values, particularly (+)-Dihydroeleutherinol, show promising potential for further development as plant-based antifungal active ingredients. However, these in silico prediction results still require validation through experimental testing to confirm their actual effectiveness, safety, toxicity, and mechanisms of action.

Based on the results of the *in silico* analysis using SwissADME in Table 3a, all secondary metabolite compounds from shallot plants demonstrated fairly good pharmacokinetic characteristics as candidates for natural antifungal agents. The analyzed parameters included water solubility, lipophilicity (LogP), and bioavailability score. Solubility is an important factor in drug compound development because it determines a compound's ability to dissolve in biological fluids, enabling optimal absorption and distribution within the body. All compounds listed in the table were categorized as having "very soluble" solubility levels, indicating good solubility in biological media. The obtained Log S values also indicated that most compounds exhibit solubility characteristics that support absorption. According to Daina et al., compounds with high solubility tend to have better pharmacokinetic profiles because they can improve the transport and distribution efficiency of active compounds within the body. Therefore, these results indicate that secondary metabolites from shallots have good potential to be developed as natural-based antifungal compounds.

The lipophilicity parameter, or Consensus Log Po/w, indicates the ability of compounds to interact with lipid membranes, including fungal cell membranes. A LogP value that is too low may make it difficult for compounds to penetrate cell membranes, whereas a value that is too high may reduce solubility and bioavailability. In the presented data, (+)-Eleutherin and (-)-Isoeleutherin exhibited moderate LogP values ranging from approximately 0.965 to 1.303, suggesting a good balance between solubility and membrane permeability. Compounds with these characteristics are generally able to penetrate biological membranes more easily and exhibit more effective pharmacological activity. In contrast, Ziganein had the highest LogP value of 3.873, indicating greater hydrophobicity than the other compounds (Daina *et al*., 2017). Compounds with moderate lipophilicity are considered ideal in drug development because they balance membrane permeability and solubility in biological fluids. Thus, most shallot compounds listed in the table possess lipophilic characteristics that sufficiently support antifungal activity.

In addition to solubility and lipophilicity, the bioavailability score parameter also showed favorable results. Nearly all compounds had bioavailability scores of 0.55–0.56, indicating a relatively high likelihood of oral absorption and systemic circulation. These values suggest that secondary metabolites from shallots may exhibit good biological efficacy if developed as

https://jurnal.rocewisdomaceh.com/index.php/roce e-ISSN : 3032-4505
Vol. 3, No. 2, Thn. 2026
https://doi.org/10.71275/roce.v3i2.208

antifungal drug candidates (Soorni *et al*., 2021). A bioavailability score of 0.55 in SwissADME analysis indicates that a compound has a reasonably good chance of exhibiting pharmacological activity after oral absorption. Good bioavailability also supports efficient distribution of compounds to biological targets, enabling optimal antifungal activity. Therefore, the bioavailability data presented in the table further strengthen the potential of shallot secondary metabolites as natural antifungal agents.

Overall, the SwissADME analysis results indicate that secondary metabolite compounds in shallot plants possess physicochemical and pharmacokinetic characteristics that support their development as natural antifungal agents. The combination of high solubility, relatively balanced lipophilicity, and favorable bioavailability scores suggests that these compounds may exhibit effective biological activity against pathogenic fungi. Compounds such as (+)-Eleutherin, (-)-Isoeleutherin, and (+)-Dihydroeleutherinol showed particularly promising profiles, demonstrating an optimal balance between solubility and membrane permeability. Nevertheless, these *in silico* results remain predictive; therefore, further in vitro and in vivo studies are required to confirm the effectiveness, safety, toxicity, and mechanisms of action of these compounds against fungal pathogens. Based on combined data from PASS Online and SwissADME analyses, it can be concluded that shallots have promising potential as a source of natural bioactive antifungal compounds.

The results of the drug-likeness analysis using SwissADME in Table 3b indicate that all secondary metabolite compounds from shallot plants fulfilled all major drug-likeness assessment parameters, namely Lipinski, Ghose, Veber, Egan, and Muegge rules. These results suggest that all compounds possess physicochemical characteristics that support their development as antifungal drug candidates. The concept of drug-likeness is used to predict whether a compound has suitable properties to be an active drug, particularly regarding absorption, distribution, metabolism, and excretion in the body (Agoni *et al.*, 2020). Drug-likeness analysis is an important stage in the development of natural product-based drugs because it helps identify compounds with a high likelihood of success in biological and pharmacological testing.

Lipinski's Rule of Five is used to assess a compound's potential for oral absorption. All compounds listed in the table complied with Lipinski's rule, indicating that they possess molecular weights, numbers of hydrogen-bond donors and acceptors, and lipophilicity values that fall within the optimal range for oral drugs. In addition, all compounds also fulfilled the Ghose and Veber rules, which are associated with molecular size, polarity, structural flexibility, and polar surface area. Compounds that meet these parameters generally exhibit good membrane permeability and oral bioavailability (Feng *et al*., 2025). stated that compliance with Lipinski, Ghose, and Veber rules indicates that a compound has a high probability of demonstrating effective biological activity with optimal absorption levels.

The Egan and Muegge parameters also showed positive results for all secondary metabolite compounds from shallots. The Egan rule is used to predict a compound's ability to penetrate biological membranes based on its polarity and lipophilicity. In contrast, the Muegge rule is used to assess the suitability of a compound's chemical structure as an active drug candidate. All compounds that satisfy these two rules indicate that shallot secondary metabolites

https://jurnal.rocewisdomaceh.com/index.php/roce e-ISSN : 3032-4505
Vol. 3, No. 2, Thn. 2026
https://doi.org/10.71275/roce.v3i2.208

possess molecular characteristics that support pharmacological activity and preliminary safety as antifungal candidates (Moldovan *et al.*, 2022). compounds that meet multiple drug-likeness parameters are more likely to succeed in the drug development process because they strike a good balance among chemical stability, permeability, and biological activity.

Overall, the drug-likeness analysis results demonstrate that all secondary metabolite compounds from shallots have very promising profiles as natural antifungal candidates. Compliance with all Lipinski, Ghose, Veber, Egan, and Muegge rules indicates that these compounds may exhibit good oral absorption, optimal membrane permeability, and molecular characteristics conducive to biological activity. These findings further strengthen previous data from PASS Online and SwissADME analyses, showing that compounds such as (+)-Eleutherin, (-)-Isoeleutherin, and (+)-Dihydroeleutherinol have strong potential for further development as natural-based antifungal agents. Nevertheless, these *in silico* results still require further validation through *in vitro* and *in vivo* studies to confirm the effectiveness, safety, toxicity, and mechanisms of action of these compounds against pathogenic fungi.

The results of the physicochemical properties analysis using SwissADME in Table 3c indicate that all secondary metabolite compounds from shallot plants exhibit physicochemical characteristics that support their development as natural antifungal candidates. Parameters such as molecular weight, heavy atoms, hydrogen bonding, molecular flexibility, topological polar surface area (TPSA), and molar refractivity significantly influence a compound's biological activity and pharmacokinetic properties. All compounds listed in the table have molecular weights ranging from 254.24 to 304.29 g/mol, which remain within the ideal range for oral drug compounds, since compounds with molecular weights below 500 g/mol are generally more easily absorbed and distributed within the body (Fagerholm, 2022). moderate molecular weight can enhance a compound's ability to penetrate biological membranes and support good oral bioavailability.

The number of aromatic atoms and the fraction Csp3 values also indicate chemical structural characteristics that support biological activity. Compounds such as Ziganein and Eleutherinol have more aromatic atoms than the other compounds, indicating a predominance of aromatic ring structures. Aromatic structures are known to play an important role in interactions between bioactive compounds and protein targets in microorganisms, including pathogenic fungi. In addition, the fraction Csp3 values of most compounds ranged from 0.07 to 0.38, indicating a balance between aromatic and aliphatic structures. Compounds with a balanced aromatic structure and good molecular flexibility tend to exhibit better chemical stability and more optimal biological activity in the development of natural product-based drugs.

The parameters for rotatable bonds, hydrogen-bond acceptors (H-bond acceptors), hydrogen-bond donors (H-bond donors), and TPSA values also showed favorable profiles. Most compounds had few rotatable bonds, ranging from 0 to 5, indicating relatively stable molecular structures with limited flexibility. Structural stability is important for enhancing specific interactions with biological targets. The TPSA values of all compounds were below 140 Å², and most were below 90 Å², indicating good membrane permeability and supporting oral absorption. Compounds with low TPSA values generally pass more readily through fungal cell membranes

https://jurnal.rocewisdomaceh.com/index.php/roce e-ISSN : 3032-4505
Vol. 3, No. 2, Thn. 2026
https://doi.org/10.71275/roce.v3i2.208

and exhibit greater biological activity (Jiang *et al*., 2025). Stated that the combination of low TPSA, balanced numbers of hydrogen bond donors and acceptors, and optimal molecular flexibility is an important indicator of a compound's success in drug development.

Overall, the physicochemical property analysis results indicate that secondary metabolites from shallot plants exhibit molecular profiles that support their antifungal activity and feasibility as natural drug candidates. Compounds such as (+)-Eleutherin, (-)-Isoeleutherin, and (-)-Hongconin demonstrated a good balance of physicochemical parameters, ranging from molecular weight and polarity to biological interaction capabilities. These characteristics support the compounds' ability to penetrate fungal cell membranes, interact with biological targets, and produce effective antifungal activity. These findings also strengthen previous PASS Online and drug-likeness data, indicating that shallot secondary metabolites have promising prospects as sources of natural antifungal compounds. Nevertheless, these *in silico* prediction results still require further validation through *in vitro* and *in vivo* studies to confirm their biological effectiveness, safety, and mechanisms of action against pathogenic fungi.

The results of the physicochemical properties analysis using SwissADME in Table 3c indicate that all secondary metabolite compounds from shallot plants exhibit physicochemical characteristics that support their development as natural antifungal candidates. Parameters such as molecular weight, heavy atoms, hydrogen bonding, molecular flexibility, topological polar surface area (TPSA), and molar refractivity significantly influence a compound's biological activity and pharmacokinetic properties. All compounds listed in the table have molecular weights ranging from 254.24 to 304.29 g/mol, which remain within the ideal range for oral drug compounds, since compounds with molecular weights below 500 g/mol are generally more easily absorbed and distributed within the body. Moderate molecular weight can enhance a compound's ability to penetrate biological membranes and support good oral bioavailability.

The number of aromatic atoms and the fraction Csp3 values also indicate chemical structural characteristics that support biological activity. Compounds such as Ziganein and Eleutherinol have more aromatic atoms than the other compounds, indicating a predominance of aromatic ring structures. Aromatic structures are known to play an important role in interactions between bioactive compounds and protein targets in microorganisms, including pathogenic fungi. In addition, the fraction Csp3 values of most compounds ranged from 0.07 to 0.38, indicating a balance between aromatic and aliphatic structures (Zeki & Mustafa, 2024). Compounds with a balanced aromatic structure and good molecular flexibility tend to exhibit better chemical stability and more optimal biological activity in the development of natural product-based drugs.

The parameters for rotatable bonds, hydrogen-bond acceptors (H-bond acceptors), hydrogen-bond donors (H-bond donors), and TPSA values also showed favorable profiles. Most compounds had few rotatable bonds, ranging from 0 to 5, indicating relatively stable molecular structures with limited flexibility. Structural stability is important for enhancing specific interactions with biological targets. The TPSA values of all compounds were below 140 Å², and most were below 90 Å², indicating good membrane permeability and supporting oral absorption. Compounds with low TPSA values generally pass more readily through fungal cell membranes and exhibit more effective biological activity. stated that the combination of low TPSA, balanced

https://jurnal.rocewisdomaceh.com/index.php/roce e-ISSN : 3032-4505
Vol. 3, No. 2, Thn. 2026
https://doi.org/10.71275/roce.v3i2.208

numbers of hydrogen bond donors and acceptors, and optimal molecular flexibility is an important indicator of a compound's success in drug development.

Overall, the physicochemical property analysis results indicate that secondary metabolites from shallot plants exhibit molecular profiles that support their antifungal activity and feasibility as natural drug candidates. Compounds such as (+)-Eleutherin, (-)-Isoeleutherin, and (-)-Hongconin demonstrated a good balance of physicochemical parameters, ranging from molecular weight and polarity to biological interaction capabilities. These characteristics support the compounds' ability to penetrate fungal cell membranes, interact with biological targets, and produce effective antifungal activity. These findings also strengthen previous PASS Online and drug-likeness data, indicating that shallot secondary metabolites have promising prospects as sources of natural antifungal compounds. Nevertheless, these *in silico* prediction results still require further validation through *in vitro* and *in vivo* studies to confirm their biological effectiveness, safety, and mechanisms of action against pathogenic fungi.

CONCLUSION

In conclusion, secondary metabolites from shallot demonstrated promising antifungal potential through PASS Online and SwissADME analyses. Compounds such as (+)-Dihydroeleutherinol, (+)-Eleutherin, and (-)-Isoeleutherin exhibited favorable biological activity, pharmacokinetic properties, and drug-likeness profiles. These findings suggest that shallot metabolites have strong potential as natural antifungal candidates for further development.

REFERENCES

A. Ibrahim, S., & F. Rizk, H. (2021). Synthesis and Biological Evaluation of Thiazole Derivatives. *Azoles - Synthesis, Properties, Applications and Perspectives*, 1–20. https://doi.org/10.5772/intechopen.93037

Aarón, R.-H., Sheila, C.-M., Julio Emmanuel, G.-P., Óscar, J.-G., Aurelio, L.-M., & Jocksan Ismael, M.-C. (2025). In Silico strategies for drug discovery: optimizing natural compounds from foods for therapeutic applications. *Discover Chemistry*, *2*(1). https://doi.org/10.1007/s44371-025-00201-3

Agoni, C., Olotu, F. A., Ramharack, P., & Soliman, M. E. (2020). Druggability and drug-likeness concepts in drug design: are biomodelling and predictive tools having their say? *Journal of Molecular Modeling*, *26*(6), 120. https://doi.org/10.1007/s00894-020-04385-6

Althubaiti, A. (2023). Sample size determination: A practical guide for health researchers. *Journal of General and Family Medicine*, *24*(2), 72–78. https://doi.org/10.1002/jgf2.600

Ayoobi, A., & Choi, H. W. (2026). In Silico Molecular Docking and Pharmacokinetic Evaluation of Cannabinoid Derivatives as Multi-Target Inhibitors for EGFR, VEGFR-1, and VEGFR-2 Proteins. *Current Issues in Molecular Biology*, *48*(2), 1–33. https://doi.org/10.3390/cimb48020204

https://jurnal.rocewisdomaceh.com/index.php/roce e-ISSN : 3032-4505
Vol. 3, No. 2, Thn. 2026
https://doi.org/10.71275/roce.v3i2.208

Borba-Santos, L. P., Nicoletti, C. D., Vila, T., Ferreira, P. G., Araújo-Lima, C. F., Galvão, B. V. D., Felzenszwalb, I., de Souza, W., de Carvalho da Silva, F., Ferreira, V. F., Futuro, D. O., & Rozental, S. (2022). A novel naphthoquinone derivative shows selective antifungal activity against Sporothrix yeasts and biofilms. *Brazilian Journal of Microbiology : [Publication of the Brazilian Society for Microbiology]*, *53*(2), 749–758. https://doi.org/10.1007/s42770-022-00725-1

Chen, Q., Yang, M., Lai, X., Hu, J., Fazal, A., Zhang, Y., Lv, X., Xiao, J., Fan, Z., Pan, Z., Yin, T., Sun, S., Lu, G., Qi, J., Lin, H., Wen, Z., Yang, Y., & Han, H. (2026). Antifungal potential of naphthoquinone derivatives: screening of shikonin-based compounds and mechanistic insights into 5,8-dihydroxy-1,4-naphthoquinone against Candida albicans in vitro and in vivo. *Microbiology Spectrum*, *14*(4), e0243825. https://doi.org/10.1128/spectrum.02438-25

Daina, A., Michielin, O., & Zoete, V. (2017). SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. *Scientific Reports*, *7*, 42717. https://doi.org/10.1038/srep42717

Elhamouly, N. A., Hewedy, O. A., Zaitoon, A., Miraples, A., Elshorbagy, O. T., Hussien, S., El-Tahan, A., & Peng, D. (2022). The hidden power of secondary metabolites in plant-fungi interactions and sustainable phytoremediation. *Frontiers in Plant Science*, *13*, 1044896. https://doi.org/10.3389/fpls.2022.1044896

Fagerholm, U. (2022). Investigation of Molecular Weights and Pharmacokinetic Characteristics of Older and Modern Small Drugs. *BioRxiv*, 2022.09.21.508888.

Feng, Q., De Chavez, D., Kihlberg, J., & Poongavanam, V. (2025). A membrane permeability database for nonpeptidic macrocycles. *Scientific Data* , *12*(1), 1–11. https://doi.org/10.1038/s41597-024-04302-z

Jiang, J., Keniya, M. V, Puri, A., Zhan, X., Cheng, J., Wang, H., Lin, G., Lee, Y.-K., Jaber, N., Zhao, C., Pang, C., Hassoun, Y., Zheng, H., Shor, E., Shi, Z., Lee, S.-H., Xu, M., Perlin, D. S., & Dai, W. (2025). Molecular landscape of the fungal plasma membrane and implications for antifungal action. *Nature Communications*, *16*(1), 9125. https://doi.org/10.1038/s41467-025-64171-x

Miebs, G., Mielniczuk, A., Kadziński, M., & Bachorz, R. A. (2024). Beyond the Arbitrariness of Drug-Likeness Rules: Rough Set Theory and Decision Rules in the Service of Drug Design. *Applied Sciences (Switzerland)*, *14*(21). https://doi.org/10.3390/app14219966

Moldovan, C., Frumuzachi, O., Babotă, M., Barros, L., Mocan, A., Carradori, S., & Crişan, G. (2022). Therapeutic Uses and Pharmacological Properties of Shallot (Allium ascalonicum): A Systematic Review. *Frontiers in Nutrition*, *9*, 903686. https://doi.org/10.3389/fnut.2022.903686

Oyejide, A. J., Adekunle, Y. A., Abodunrin, O. D., & Atoyebi, E. O. (2025). Artificial intelligence, computational tools and robotics for drug discovery, development, and delivery. *Intelligent Pharmacy*, *3*(3), 207–224. https://doi.org/10.1016/j.ipha.2025.01.001

Pogodin, P. V, Lagunin, A. A., Rudik, A. V, Filimonov, D. A., Druzhilovskiy, D. S., Nicklaus, M. C., & Poroikov, V. V. (2018). How to Achieve Better Results Using PASS-Based Virtual Screening: Case Study for Kinase Inhibitors. *Frontiers in Chemistry*, *6*, 133. https://doi.org/10.3389/fchem.2018.00133

https://jurnal.rocewisdomaceh.com/index.php/roce e-ISSN : 3032-4505
Vol. 3, No. 2, Thn. 2026
https://doi.org/10.71275/roce.v3i2.208

Prabawati, S., Widayanti, S. M., Sulistyaningrum, A., Setyadjit, S., Arif, A. Bin, Winarti, C., Jamal, I. B., Munarso, S. J., Waryat, W., Budiyanto, A., & Risfaheri, R. (2026). Physiology, Nutrition, and Postharvest Technology on Shallots (Allium cepa L. aggregatum): A Review. *Scientifica*, *2026*(1), 8328535. https://doi.org/https://doi.org/10.1155/sci5/8328535

Roney, M., & Mohd Aluwi, M. F. F. (2024). The importance of in-silico studies in drug discovery. *Intelligent Pharmacy*, *2*(4), 578–579. https://doi.org/10.1016/j.ipha.2024.01.010

Sadybekov, A. V, & Katritch, V. (2023). Computational approaches streamlining drug discovery. *Nature*, *616*(7958), 673–685. https://doi.org/10.1038/s41586-023-05905-z

Sharma, A., Raut, S. S., Shukla, A., Singh, A., & Mishra, A. (2026). Therapeutic targeting of the mitochondrial dysfunction-PANoptosis axis: Mechanistic insights and emerging strategies. *Translational Research*, *291*, 1–39. https://doi.org/https://doi.org/10.1016/j.trsl.2026.03.004

Soorni, A., Akrami, A. M., Abolghasemi, R., & Vahedi, M. (2021). Transcriptome and phytochemical analyses provide insights into the organic sulfur pathway in Allium hirtifolium. *Scientific Reports*, *11*(1), 1–13. https://doi.org/10.1038/s41598-020-80837-6

Tanwar, S., Kalra, S., & Bari, V. K. (2024). Insights into the role of sterol metabolism in antifungal drug resistance: a mini-review. *Frontiers in Microbiology*, *15*, 1409085. https://doi.org/10.3389/fmicb.2024.1409085

van Rhijn, N., & Rhodes, J. (2025). Evolution of antifungal resistance in the environment. *Nature Microbiology*, *10*(8), 1804–1815. https://doi.org/10.1038/s41564-025-02055-y

Wang, B., Liu, Q., Zhao, W., Zhang, T., Zhang, D., Sutcharitchan, C., & Li, S. (2026). Revolutionizing drug discovery from natural products: The roles of artificial intelligence and multi-omics in accelerating innovation. *Acta Pharmaceutica Sinica B*, (xxx). https://doi.org/10.1016/j.apsb.2025.12.030

Zeki, N. M., & Mustafa, Y. F. (2024). Digital alchemy: Exploring the pharmacokinetic and toxicity profiles of selected coumarin-heterocycle hybrids. *Results in Chemistry*, *10*, 101754. https://doi.org/https://doi.org/10.1016/j.rechem.2024.101754

Zhang, S., Liu, K., Liu, Y., Hu, X., & Gu, X. (2025). The role and application of bioinformatics techniques and tools in drug discovery. *Frontiers in Pharmacology*, *16*(February), 1–12. https://doi.org/10.3389/fphar.2025.1547131