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Computational Study of Household Plants as Immunomodulators on *Human Metapneumovirus*

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Abstract: Human metapneumovirus (HMPV) is a causative agent of acute lower respiratory tract infections, especially in children. Until now, there are not many natural-based immunomodulatory therapies available. This study aims to explore the potential of household plants from the *Syzygiumand zingiber* Genus as immunomodulators against HMPV using computational studies. The target receptor used is RNA-dependent RNA polymerase (RdRp), a vital enzyme in HMPV genome replication. The methods used include molecular docking, validation of biological activity through Way2Drug and evaluation of pharmacokinetic feasibility using Lipinski's Rule of Five. Based on the docking results, the compounds with the strongest binding affinity are myricetin (-8.3 kcal/mol) from the Syzygiumgenus and 10-gingerdione (-7.2 kcal/mol) from the Zingiber genus. Based on the Way2Drug assay results, myricetin compounds from the Syzygiumgenus showed the strongest antioxidant potential (Pa 0.924). In the Zingiber Genus, the compound 10- gingerdione showed the highest antiviral value (Pa 0.434). Based on the Lipinski's Rule of Five analysis, quercetin from the Syzygiumgenus and 10-gingerol from the Zingiber genus fulfilled all five criteria. Both showed high potential as natural immunomodulatory agents against HMPV, confirming that secondary metabolites from household plants deserve further research as natural immunomodulators.

Keywords: computational study, *Human metapneumovirus*, immunomodulator, Syzygium, Zingiber

Abstrak: *Human metapneumovirus (HMPV) merupakan agen penyebab infeksi saluran pernapasan bawah akut, terutama pada anak-anak. Hingga kini, belum banyak tersedia terapi immunomodulator berbasis alami. Penelitian ini bertujuan mengeksplorasi potensi tanaman rumah tangga dari Genus Syzygiumdan Zingiber sebagai immunomodulator terhadap HMPV menggunakan studi komputasi. Target reseptor yang digunakan adalah RNA- dependent RNA polymerase (RdRp), enzim vital dalam replikasi genom HMPV. Metode yang digunakan meliputi penambatan molekul, validasi aktivitas biologis melalui Way2Drug, dan evaluasi kelayakan farmakokinetik menggunakan Lipinski's Rule of Five. Berdasarkan hasil penambatan molekul, senyawa dengan ikatan afinitas terkuat yaitu myricetin (-8,3 kcal/mol) dari Genus Syzygiumdan 10-gingerdione (-7,2 kcal/mol) dari Genus Zingiber. Berdasarkan hasil uji Way2Drug, senyawa myricetin menunjukkan potensi antioksidan terkuat (Pa 0,924), dan senyawa 10-gingerdione menunjukkan nilai antivirus tertinggi (Pa 0,434). Berdasarkan analisis Lipinski's Rule of Five, senyawa quercetin [1.1][LE1.2]dari Genus Syzygiumdan 10-gingerol dari Genus Zingiber memenuhi seluruh lima kriteria. Keduanya menunjukkan potensi tinggi sebagai agen immunomodulator alami terhadap HMPV, menegaskan bahwa metabolit sekunder dari tanaman rumah tangga layak diteliti lebih lanjut sebagai immunomodulator alami.*

Kata kunci: *Human metapneumovirus, immunomodulator, studi komputasi, Syzygium, Zingiber*

INTRODUCTION

Respiratory tract infections are the second leading cause of mortality among children under five years of age. *Human metapneumovirus* (HMPV) is one of the primary biological agents responsible for the transmission and development of acute lower respiratory tract infections. HMPV infection may lead to complications such as bronchitis, bronchiolitis, and pneumonia (Geiser *et al*. 2021). HMPV was first identified in 2001 from 28 children in the Netherlands who were diagnosed with acute respiratory tract infections (Ma *et al.* 2023).

According to data from the Indonesian Ministry of Health, HMPV re-emerged in January 2025, with 79 confirmed cases reported in Indonesia, particularly in the Jakarta region (Kementerian Kesehatan Republik Indonesia 2025). HMPV is a negative-sense single-stranded RNA virus belonging to the family Pneumoviridae and predominantly infects both the upper and lower respiratory tracts (Satapathy *et al.* 2025). RNA (*ribonucleic acid*) is a type of nucleic acid that functions as a carrier of genetic information for gene expression. Unlike most organisms, certain viruses utilize RNA as their primary genetic material.

In HMPV, RdRp is a vital enzyme involved in viral genome replication and transcription. Following viral entry into the host cell, RdRp catalyzes the synthesis of viral genomic RNA for replication and the production of viral mRNA, which is subsequently translated into structural and non-structural proteins. Due to its central role, RdRp represents a promising molecular target for antiviral drug development, either through inhibition of its enzymatic activity or by preventing ligand or substrate binding at its active site. Currently, there is no officially approved therapeutic treatment specifically targeting HMPV. However, recent studies suggest that several FDA-approved broad-spectrum antiviral drugs, such as remdesivir and peramivir, may serve as potential therapeutic candidates against HMPV. Nevertheless, these antiviral agents still require further investigation and structural optimization to enhance their efficacy (Dubey *et al.* 2025).

Household plants are commonly cultivated domestic plants, some of which contain compounds believed to provide health benefits. These plants are generally easy to maintain, possess aesthetic value, and can function as household ornaments. Many household plants with medicinal properties are traditionally used as emergency herbal remedies. Examples include plants from the genus *Zingiber* (family *Zingiber*aceae) and genus *Syzygium* (family Myrtaceae). These plants are widely favored for home cultivation due to their ease of harvesting and low maintenance costs. According to the literature, compounds present in ginger are known to exhibit various biological activities, including antioxidant and antiviral properties. Previous computational studies have demonstrated that bioactive compounds found in ginger, such as *ar-curcumene*, gingerol, geraniol, shogaol, *Zingiber*ene, *gingerenone*, and *zingiberenol*, can act as ligands capable of interfering with the interaction between viral spike (S) proteins and the ACE2 receptor on human cells (Deng *et al.* 2022). Consequently, ginger is predicted to inhibit viral infection processes in human host cells.

In addition to ginger, another household plant predicted to contain antiviral antagonistic compounds is bay leaf (*Syzygium*genus). Bay leaves contain approximately 17% essential oil, with eugenol and *methyl chavicol* as the primary constituents. Previous *in vivo* and *in vitro* studies have shown that eugenol can inhibit viral replication, supported by a favorable binding affinity value of 6.3 kcal/mol against viral protease targets (Dewi & Riyandari 2020). Based on the literature concerning viral respiratory infections, consumption of herbal plants is believed to stimulate immune responses and modulate inflammation, thereby enhancing immune system function. Bioactive compounds in plants that enhance immune activity are referred to as immunomodulators, including hirtetralin, niranthin, hypophyllantin, phylltetralin, pyropheophorbide, gingerol, anthocyanins, xanthones, and flavonoids (Aziz *et al.* 2020). Natural plant-derived immunomodulators are considered safer than synthetic immunomodulatory drugs due to their milder side effects (Hidayah & Indradi 2020).

Currently, researchers are actively investigating the immunomodulatory potential of herbal plants using computational molecular approaches. Therefore, this article presents a computational study on the potential of secondary metabolite compounds from *Syzygium*and *Zingiber* species as immunomodulators against HMPV. The exploration of natural bioactive compounds as therapeutic and preventive agents for infectious diseases aligns with the Sustainable Development Goals (SDGs), particularly Goal 3, which aims to ensure healthy lives and promote well-being for all. The objective of this study is to determine the binding affinity values of selected secondary metabolite compounds from the *Syzygium*and *Zingiber* genera against the RdRp receptor, to evaluate their antiviral activity using the Way2Drug platform, and to assess their drug-likeness eligibility as immunomodulatory candidates based on Lipinski's Rule of Five. This research supports efforts to develop plant-based immunomodulators against HMPV derived from household plants.

MATERIALS AND METHOD

Materials

The materials that are used in this research were secondary metabolites compounds on plants that are included in genus Syzygium, namely *Syzygium aromaticum, S. cumini, S. jambos, Zingiber officinale,* dan *Z. montanum.* The computational analysis of the compounds was performed using PyRx and Discovery Studio in an 64bit *HP laptop* with the processor of Intel(R) Core(TM) i3-N305. Additional databases and web tools are used for supporting the analysis performed, such as PubChem, NCBI, Way2Drug, Dr. Duke Phytochemical Database, and Lipinski's Rule of Five.

Method

Data collecting was conducted by secondary data collection method, with the main method being literature study and in-silico computation simulation (molecular docking). The data collecting was first conducted by doing the literature review on or related to secondary metabolite compounds found in plants

of the Genera *Syzygium*and *Zingiber*. Afterwards, the acknowledgement on the pytochemical component of said plants are acquired via phytochemical database website, such as Dr. Duke's Phytochemical Database. The data and structure of plant's secondary metabolites was acquired via PubChem, RCSB PDB, and NCBI. Thereafter, the molecular docking was conducted primarily via softwares, such as Discovery Studio (for water removal and 2D/3D structural view of the secondary metabolites) and PyRx via ina wizard (for docking). This molecular docking was conducted to predict the interaction between secondary metabolite compounds from *Syzygium*and *Zingiber* plants and RdRp receptors from HMPV. The data analysis are conducted after the results are given by the software, which includes the binding affinity and the binding energy of the docking result. This data were analyzed to determine the value of the potential biological activitiy of the compounds. The prediction of the potential biological acctivity of the compounds are predicted via Way2Drug portal (https://www.way2drug.com/passonline/), while the evaluation of the suitability of compounds as drugs are evaluated and analyzed via Lipinski's rule of Five portal (https://scfbio-iitd.res.in/software/drugdesign/lipinski.jsp), which specifically used after the chemical structures obtained via PubChem website.

RESULTS AND DISCUSSION

Secondary Metabolite Compounds in *Syzygiumand zingiber* Plants

Exploration of the Dr. Duke's Phytochemical and Ethnobotanical Databases (https://phytochem.nal.usda.gov/) and PubChem (https://pubchem.ncbi.nlm.nih.gov) identified 13 secondary metabolite compounds, which are listed in Tables 1 and 2. The results of exploration on Dr. Duke's Phytochemical and Ethnobotanical Databases (https://phytochem.nal.usda.gov/) and PubChem (https://pubchem.ncbi.nlm.nih.gov) websites found

Table 1. Secondary metabolite compounds in *Syzygium*sp. Plants.

Species	Compound	CID
Syzygiumcumini	Gallic acid	370
	Myricetin	5281672
	Quercetin	5280343
	Kaempferol	5280863
Syzygiumaromaticum	Gallic acid	370
	Kaempferol	5280863
	Myricetin	5281672
	Quercetin	5280343
	Linalool	6549
Syzygiumjambos	Myricetin	5281672
	Quercetin	5280343
	Gallic acid	370
	Linalool	6549

Table 2. Secondary metabolite compounds in *Zingiber* sp. Plants.

Species	Compound	CID
Zingiber officinale	10-Gingerol	168115
	10-Shogaol	6442612
	10-Gingerdione	14440539
	Humulene	5281520
	Zingiberene	92776
Zingiber montanum	Zerumbone	5470187
	(E)-1-(3,4-Dimethoxyphenl)butadiene (DMPBD)	11528492
	(E)-4-(4-hydroxy-3-methoxyphenyl)- but-3-en-1-yl acetat (coniferyl acetate)	23725772

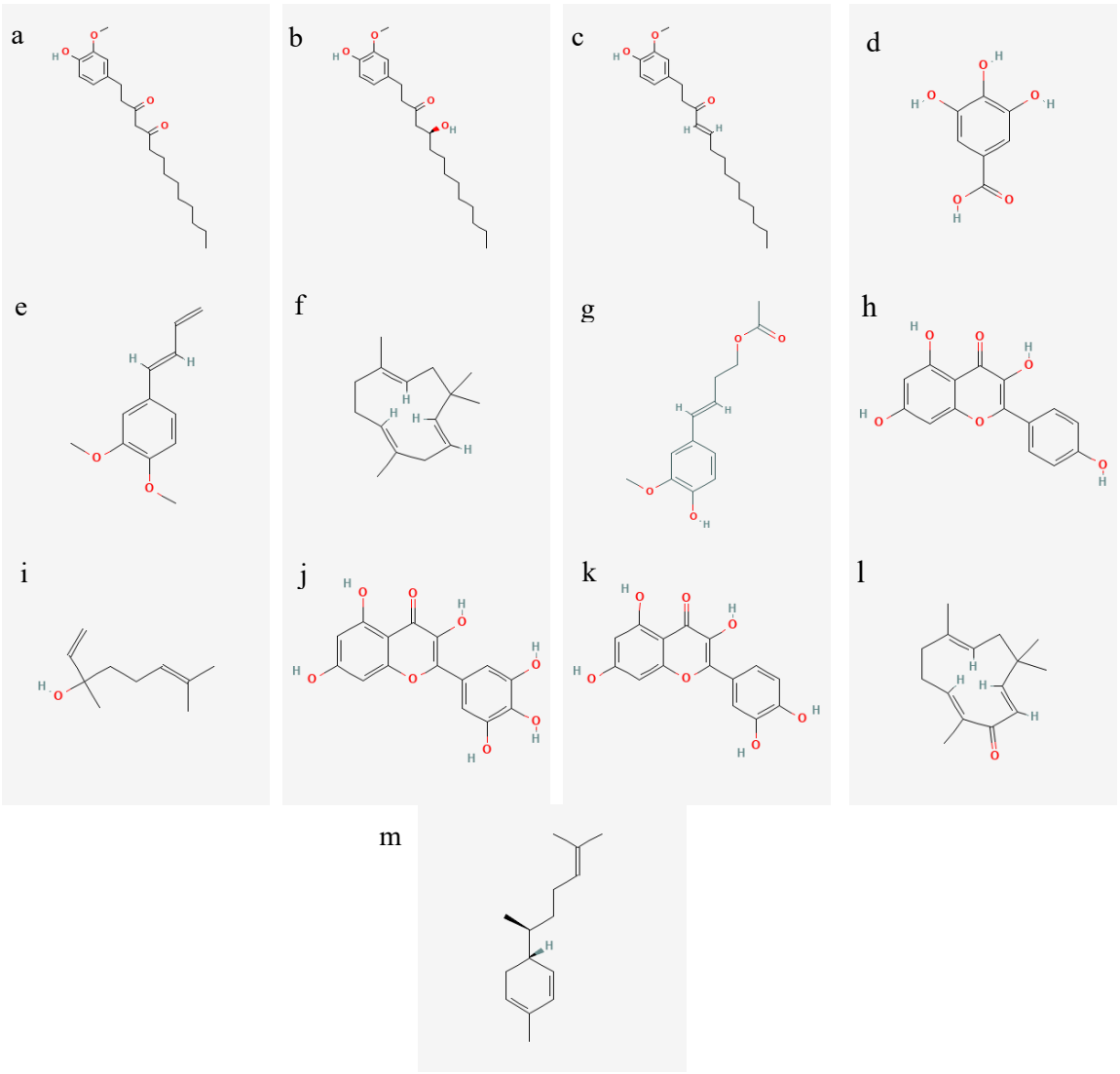

Figure 2. 2D structures of secondary metabolite compounds: (a) 10-Gingerdione; (b) 10-Gingerol; (c) 10-Shogaol; (d) Gallic acid; (e) (E)- 1-(3,4-DMPBD); (f) Humulene; (g) Coniferyl acetate; (h) Kaempferol; (i) Linalool; (j) Myricetin; (k) Quercetin; (l) Zerumbone; (m) Zingiberene

13 types of secondary metabolite compounds listed in Table 1 and Table 2.

Figure 2 illustrates the three-dimensional (2D) structures of each selected secondary metabolite compound derived from *Syzygium*sp. and *Zingiber* sp. Clear differences in chemical structures are observed, including the number and position of hydroxyl (–OH) groups, carbon chains, and aromatic rings, all of which determine the biological activity of each compound. This structural diversity strongly influences the function and biological activity of the individual metabolites.

Preparation of 3D Structures of Protein and Ligands

Figure 3(a) shows the 3D representation of the RdRp protein without a bound ligand . The structure consists of alpha helices (displayed as red ribbons), beta sheets (blue), and connecting loops (typically shown as green or gray ribbons). HMPV fusion (F) protein is a class I viral fusion glycoprotein with a structure that is predominantly α-helical. The major α-helical regions are located in the heptad repeat A (HRA) and heptad repeat B (HRB) domains, which refold into a stable six-helix bundle during membrane fusion. α-heliceHMPV F protein also contains a moderate proportion of β-sheet structures, mainly localized within the globular head and antigenic domains. These β-strands contribute to structural stabilization of surface-exposed epitopes and receptor-interacting regions. α-helical contribute approximately 45-55% of the protein's secondary structure, making it the dominant structural feature, while the β-sheet content is estimated to account for approximately 10-15% of the total secondary structure (Battles *et al.* 2017).

This protein is a crucial component of the HMPV and plays a key role in viral RNA genome replication

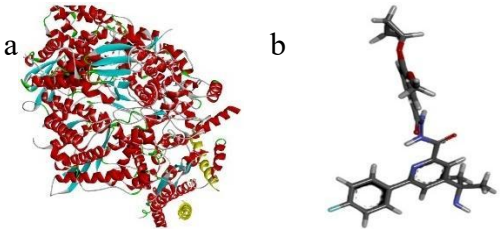

Figure 3. (a) Structure of RdRp receptor chain (8FPJ) without native ligand; (b) Native ligand RdRp

within the host cell. According to data from the Research Collaboratory for Structural Bioinformatics

Protein Data Bank (RCSB PDB), the RdRp structure (8FPJ) has a resolution of 2.74 Å. This value reflects the resolution achieved by electron microscopy, indicating the level of structural detail obtained; smaller Å values correspond to higher resolution and accuracy. A study by Yin *et al*. (2020) supports the achievement of high-resolution structures in RdRp complex studies, reporting an apo RdRp complex (nsp12–nsp7–nsp8) of SARS-CoV-2 at a resolution of 2.8 Å, which is also considered high resolution.

Figure 3(b) presents the 3D chemical structure of the native ligand, a small natural molecule that binds to the active site of RdRp. This ligand is typically a nucleotide or its analog that serves as a substrate in the RNA polymerization reaction. The native ligand is essential because it occupies the RdRp active site, interacts with key amino acid residues, and supports the enzyme's catalytic function.

Molecular Docking Analysis

Based on molecular docking analysis of 13 active compounds identified in *Syzygium*sp. and *Zingiber* sp., varying binding affinity values were obtained against the HMPV target protein. More negative binding affinity values indicate stronger interactions between the ligand and receptor (Raizma *et al*. 2025).

Table 3 presents the docking results of six secondary metabolites from *Syzygium*sp. against the HMPV RdRp enzyme. Myricetin exhibited the highest binding affinity (-8.3 kcal/mol), followed by quercetin (-7.8 kcal/mol) and kaempferol (-7.7 kcal/mol), indicating strong binding affinity to the RdRp active site. These three compounds are flavonoids known to be promising candidates for antiviral and immunomodulatory activity. Several studies have reported that the SARS-CoV helicase protein can be inhibited by myricetin through interference with ATPase activity (Batistuta *et al*. 2021). Quercetin has been shown to block viral entry and replication and to accelerate viral clearance (Rizky *et al*. 2022). Kaempferol has been reported to inhibit hMPV by suppressing RNA polymerase activity, reducing viral replication, and enhancing the human immune response, making it useful in combating hMPV infection (Ganguly *et al*. 2025). In addition, gallic acid and linalool exhibited moderate binding affinities of -5.8 and -5.1 kcal/mol, respectively, while oxalic acid showed the lowest binding affinity (-3.6 kcal/mol), indicating weak potential interactions. These results further support the potential of flavonoids from *Syzygium*sp., particularly myricetin, quercetin, and kaempferol, as natural candidates for the development of antiviral agents against HMPV.

Molecular docking results presented in Table 4 for eight secondary metabolites from *Zingiber* sp. showed that 10-gingerdione had the highest binding affinity (-7.2 kcal/mol), followed by 10-shogaol and *Zingiber*ene (each -7.1 kcal/mol), and 10-gingerol (-7.0 kcal/mol). A study by Ahkam *et al*. (2020) reported that compounds such as gingerol and shogaol can inhibit viral protease activity through interactions with enzyme active sites that are essential for viral replication. Compounds such as coniferyl acetate, (E)-1-(3,4-DMPBD), zerumbone, and humulene exhibited relatively lower binding affinity values (-6.4 to -5.9 kcal/mol) compared to major compounds such as 10-gingerdione or 10-gingerol, indicating less stable interactions with the HMPV RdRp enzyme. Nevertheless, these compounds still show potential as supportive agents in viral inhibition due to their synergistic effects when combined with other active compounds and their contributions to other biological activities, including antioxidant, anti-inflammatory, and immune-stimulating effects. Zerumbone and humulene are known for their antipyretic, anti-inflammatory, anti-ulcer, analgesic, and antimicrobial properties (Sayuti & Atikah 2022).

Way2Drug Analysis

The Way2Drug platform (https://www.way2drug.com/passonline/) was used to predict the potential biological activities of compounds based on their chemical structures, particularly antiviral and antioxidant activities. The main parameters used were Pa (probability of activity) and Pi (probability of inactivity). Generally, compounds with Pa values greater than 0.7 are considered to exhibit strong and well-established biological activity, whereas compounds with Pa values between 0.3 and 0.7 are considered to have potential activity, possibly reflecting novel or less-studied chemical structures (Table 5).

Table 3. Docking results of *Syzygium*sp. secondary metabolite compounds on the RdRp Receptor of the HMPV

Compounds	*Binding affinity* (kcal/mol)
Myricetin	-8.3
Quercetin	-7.8
Kaempferol	-7.7
Gallic acid	-5.8
Linalool	-5.1
Oxalic acid	-3.6

Table 4. Docking results of *Zingiber* sp. secondary metabolite compounds on the RdRp receptor of the HMPV virus

Compounds	*Binding affinity* (kcal/mol)
10-Gingerdione	-7.2
10-Shogaol	-7.1
*Zingiber*ene	-7.1
10-Gingerol	-7.0
Coniferyl acetate	-6.4
(E)-1-(3,4-DMPBD)	-5.9
Zerumbone	-5.9
Humulene	-5.9

Analysis of the *Syzygium*genus showed that myricetin, quercetin, and kaempferol found in *S. cumini*, *S. aromaticum*, and *S. jambos* exhibited strong antioxidant potential. The Pa values for antioxidant activity were 0.924 for myricetin, 0.872 for quercetin, and 0.856 for kaempferol, with very low Pi values (<0.01), indicating high stability and effectiveness of their bioactivities. For antiviral activity, these compounds exhibited Pa values ranging from 0.260 to 0.334, which are sufficiently significant to support their potential as herbal immunotherapeutic agents. These findings are consistent with the study by Singh *et al*. (2020), which reported strong binding affinities of myricetin and quercetin to SARS-CoV-2 RdRp, with binding energies of -7.2 and -6.9 kcal/mol, respectively, highlighting their potential as effective RdRp inhibitors. Overall, these results suggest that flavonoid compounds from the *Syzygium*genus have considerable potential as therapeutic agents in the development of herbal therapies based on molecular approaches and local wisdom.

In the *Zingiber* genus, 10-gingerdione exhibited the highest Pa value for antiviral activity (0.434), followed by 10-gingerol (0.277) and 10-shogaol (0.262). Although these values are moderate, they remain functionally relevant in herbal-based therapeutic approaches. For antioxidant activity, 10-shogaol showed the highest potential (Pa = 0.472), followed by 10-gingerdione (Pa = 0.388) and 10-gingerol (Pa = 0.366). Other compounds, such as coniferyl acetate and (E)-1-(3,4-DMPBD), also showed relatively good antioxidant Pa values (0.395 and 0.407, respectively), indicating that phenolic and sesquiterpenoid components of *Zingiber* possess capacity as natural immunomodulators.

Lipinski's Rule of Five Analysis

The Lipinski's Rule of Five portal (https://scfbio.iitd.res.in/software/drugdesign/lipinski.jsp) was used to evaluate the suitability of secondary metabolite compounds as orally administered drug candidates based on their chemical properties. Key parameters include molecular weight, number of hydrogen bond donors and acceptors, logP, and molar refractivity. According to the Lipinski's Rule of Five, drug-like compounds should have a molecular weight below 500 Da, lipophilicity expressed as logP below 5, fewer than 5 hydrogen bond donors, fewer than 10 hydrogen bond acceptors, and molar refractivity between 40 and 130 (Rai *et al.* 2023). Compounds that violate no more than one rule are considered to have high potential for good oral absorption.

Based on the data in Table 6, within the *Syzygium*genus, myricetin, quercetin, kaempferol, gallic acid, and linalool exhibited characteristics suitable as drug candidates. Myricetin (318 Da, logP 1.7) and quercetin (302 Da, logP 2.0) m*et al*l Lipinski criteria. Both compounds have hydrogen bond donors and acceptors within acceptable limits (quercetin: 5 donors and 7 acceptors; myricetin: 6 donors and 8 acceptors), indicating strong binding affinity to target

Table 5. Results of the Way2Drug analysis of secondary metabolite compounds

Species	Compounds	*Way2Drug*			
		Antiviral		Antioxidant	
		Pa	Pi	Pa	Pi
S. cumini	Gallic acid	0.342	0.025	0.520	0.006
	Myricetin	0.334	0.026	0.924	0.003
	Quercetin	0.262	0.053	0.872	0.003
	Kaempferol	0.260	0.054	0.856	0.003
S. aromaticum	Gallic acid	0.342	0.025	0.520	0.006
	Kaempferol	0.260	0.054	0.856	0.003
	Myricetin	0.334	0.026	0.924	0.003
	Quercetin	0.262	0.053	0.872	0.003
	Linalool	0	0	0.380	0.140
S. jambos	Myricetin	0.334	0.026	0.924	0.003
	Quercetin	0.262	0.053	0.872	0.003
	Asam Galat	0.342	0.025	0.520	0.006
	Linalool	0	0	0.380	0.140
S. officinale	10-Gingerol	0.277	0.045	0.366	0.015
	10-Shogaol	0.262	0.053	0.472	0.008
	10-Gingerdione	0.434	0.011	0.388	0.013
	Humulene	0.200	0.096	0	0
	*Zingiber*ene	0	0	0.234	0.041
Z. montanum	Zerumbone	0	0	0.153	0.100
	(E)-1-(3,4-DMPBD)	0	0	0.407	0.011
	asetat koniferil	0.162	0.145	0.395	0.013

proteins through hydrogen bonding interactions. Gallic acid, with a molecular weight of 170 Da and logP of 0.5, has 4 donors and 5 acceptors, supporting its strong antioxidant capacity via hydrogen donation. Linalool, with a molecular weight of 154 Da and logP of 2.6, also meets all Lipinski criteria, indicating its potential as a drug-like compound.

Within the *Zingiber* genus, 10-gingerol, 10-shogaol, and 10-gingerdione demonstrated suitable drug-like characteristics. All three compounds have molecular weights below 500 Da and hydrogen bond donor–acceptor values within Lipinski limits; however, two of them slightly exceeded the logP threshold. Specifically, 10-shogaol and 10-gingerdione have logP values of 5.5 and 5.4, respectively, which marginally exceed the limit but remain within acceptable tolerance. Humulene, *Zingiber*ene, and zerumbone exhibited high logP values (>4.2) with minimal hydrogen bond donors and acceptors (0–1). Although their hydrogen bonding capacity is low, these compounds exhibit high membrane permeability. Compounds such as (E)-1-(3,4-DMPBD) and coniferyl acetate showed acceptable logP values, appropriate donor and acceptor counts, and molecular weights below 500 Da, supporting favorable distribution and bioactivity, including antioxidant and anti-inflammatory effects.

Overall, Lipinski's Rule of Five analysis showed that six compounds met all five criteria (linalool, 10-gingerol, *Zingiber*ene, zerumbone, (E)-1-(3,4-DMPBD), and coniferyl acetate). Six compounds met four criteria (gallic acid, myricetin, quercetin, 10-shogaol, 10-gingerdione, and humulene), while one compound (kaempferol) met only one criterion. The Lipinski's Rule of Five serves as a predictive guideline for evaluating oral drug-likeness based on pharmacokinetic properties; however, it does not absolutely reflect the pharmacological potential of secondary metabolites, which often possess complex structures yet still exhibit high therapeutic activity. The rule primarily relates to oral drug administration and is associated with absorption and distribution processes (Nuraini & Ruswanto 2021).

Several additional factors support the consideration of a compound as a potential antiviral agent, including viral inhibition activity observed *in vitro*, effectiveness and safety in biological systems through *in vivo* or *in ovo* testing, high selectivity indices, and immunostimulatory effects. The more hierarchical testing stages conducted (computational, *in vitro*, *in ovo*, *in vivo*), the stronger the evidence

Table 6. Results of the Lipinski's Rule of five test on secondary metabolite compounds

Species	Compound	*Lipinski's Rule of Five*				
		Mass	***Donor***	***Acceptor***	***LogP***	***Molar Refractivity***
S. cumini	Gallic acid	170	4	5	0.5	38
	Myricetin	318	6	8	1.7	75
	Quercetin	302	5	7	2	74
	Kaempferol	594	9	15	-1.5	135
S. aromaticum	Gallic acid	170	4	5	0.5	38
	Kaempferol	594	9	15	-1.5	135
	Myricetin	318	6	8	1.7	75
	Quercetin	302	5	7	2	74
	Linalool	154	1	1	2.6	49
S. jambos	Myricetin	318	6	8	1.7	75
	Quercetin	302	5	7	2	74
	Gallic acid	170	4	5	0.5	38
	Linalool	154	1	1	2.6	49
Z. officinale	10-Gingerol	350	2	4	4.7	101
	10-Shogaol	332	1	3	5.5	99
	10-Gingerdione	348	2	4	5.4	101
	Humulene	204	0	0	5	68
	*Zingiber*ene	204	0	0	4.8	68
Z. montanum	Zerumbone	218	0	1	4.2	69
	(E) -1- (3,4-DMPBD)	190	0	2	2.9	58
	Coniferyl acetate	236	1	4	2.3	64

supporting further development of a compound as an antiviral agent (Nuraini & Ruswanto 2021). Previous *in vitro* studies demonstrated that myricetin exhibits strong antiviral activity against Ebola virus by inhibiting VP35–dsRNA interactions, with an IC_{50} value of 2.7 µM. Other studies have shown that myricetin and quercetin possess strong antiviral activity against Zika virus by targeting viral replication, with IC_{50} values of 0.58 ± 0.17 µM for myricetin and a CC_{50} value >500 mM in Vero cells (Agrawal *et al*. 2023). Chang *et al*. (2024) reported that gallic acid inhibits Influenza A H1N1 virus replication in A549 lung epithelial cells without inducing toxicity by significantly reducing viral M1 and M2 protein production and inhibiting infection-induced autophagosome accumulation.

Numerous bioactive compounds from the *Zingiber* genus, particularly *Zingiber officinale* and *Zingiber montanum*, have demonstrated promising antiviral activity through *in vitro*, *in vivo*, and *in silico* studies. Hayati *et al*. (2021) reported that 10-gingerol inhibits Chikungunya virus (CHIKV) replication with an IC_{50} value of 0.031 mM and more than 95% viral titer reduction without significant cellular toxicity. Another study by Haridas *et al*. (2021) identified compounds such as (6)-gingerol, (8)-gingerol, (10)-gingerol, (10)-shogaol, (8)-paradol, and (10)-paradol as potential viral entry inhibitors through interactions with the spike receptor-binding domain (RBD) and the human ACE2 receptor. In addition, α-humulene has been reported to exhibit virucidal activity against Bovine Viral Diarrhea Virus (BVDV), showing a significant reduction in viral

titers after *in vitro* incubation at a concentration of 100 μM.

CONCLUSION

Based on the results of the molecular docking simulation, the secondary metabolite compounds showed the strongest binding affinity values against the HMPV virus RdRp, namely myricetin (*Syzygium*genus) and 10-gingerdione (*Zingiber* genus). Based on the potency test results from Way2Drug, the myricetin compound showed very strong antioxidant potential, indicating its capability as a herbal-based immunotherapy agent. The 10-gingerdione compound showed the highest antiviral value, while 10-shogaol had the highest antioxidant activity value. Based on the Lipinski's Rule of Five analysis, all compounds met several criteria as drug compounds, but only the quercetin compound from the *Syzygium*genus and 10-gingerol from the *Zingiber* genus fulfilled all pharmacokinetic criteria.

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