In Silico Analysis of the Inhibitory Potential of *Zingiber Officinale* Roscoe Compounds Against SARS-CoV-2

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Abstract. In traditional medicine, *Z. officinale* has been known and used for centuries. However, with the current ongoing COVID-19 pandemic, *Z. officinale* is increasingly being used to treat symptoms of COVID-19 and increase overall immunity. The presence of multiple phytochemicals contained in *Z. officinale* has been widely reported. In this study, we tried to observe the inhibitory activity of the chemical constituents in *Z. officinale* against SAR-CoV-2. We used the main protease COVID-19 receptor which obtained from a protein data bank coded PDB ID 6LU7, to tether the active compound within *Z. officinale*. Protease is a protein that can represent a target for inhibition of viral replication or transcription. Proteases are widely used in the treatment of viruses since viral replication generally occurs with the aid of proteases. Currently proteases are widely used in the development of antiviral therapy and as a target protein. Evaluation of the inhibitory effect of the active compound in *Z. officinale* on the protein was performed. The molecular docking results of the 60 chemical compounds contained within *Z. officinale* showed that there were 2 chemical compounds in *Z. officinale*, Zingeberene and Lariciresinol that had the highest activity against the protein. Overall, fifteen of the 60 analyze by the molecular docking test showed the ability to inhibit protease protein. The molecular docking simulation showed that *Z. officinale* has activity against the SARS-CoV-2 PDB 6LU7 protein. The biological activity of potential active compounds in *Z. officinale* against SARS-CoV-2 and its associated mechanisms of action must be investigated further.

Keywords: *Z. officinale* Roscoe · molecular docking · inhibitory activity SAR-CoV-2

1 Introduction

Zingiber officinale Roscoe better known as ginger, is generally used as a cold medicine to treat colds, aches and pains and is often mixed with other herbs to make herbal medicine. *Z. officinale* has been widely reported to be efficacious against numerous symptoms and diseases, including motion sickness [1, 2], diabetes mellitus [3], obesity [4], antioxidants

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[5], neuropathic pain [6], neuro-modulatory effects [7], hepatoprotector [8], antibacterial [9], anticancer [10], cardiovascular [11], anti-proliferative/cancer chemo therapeutics [12], antiviral [13, 14]. It has been reported that more than 50 chemical compounds with medicinal potential have been identified in *Z. officinale* [6, 9, 15–21]. However, pharmaco dynamics studies of herbs have shown that active compounds play a role in the mechanism of a treatment, relying on the synergies between the compounds to produce the mechanism, making it difficult to identify the herbal mechanism against a target disease [22].

The Corona virus Disease 2019 (COVID-19) pandemic has hit almost all the countries of the world. Every day hundreds and thousands of people die because of COVID-19, including in Indonesia. People have tried to use various drugs to treat COVID-19 and have also resorted to herbal medicine. *Z. officinale* is one of the herbs used to increase endurance in Indonesia. In addition, it is also used by COVID-19 patients to accelerate the healing process even though the treatment mechanism is uncertain.

SARS-CoV-2 is a virus that belongs to the family Corona viridae, similar to previous outbreaks such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrom (SARS). The SARS-CoV-2, began spreading at the end of 2019 in Wuhan China. The virus is a new type of virus that had never been previously identified. SARS-CoV-2 much like the SARS virus, has host cell receptors that have the same function as Angiotensin Converting Enzyme 2 (ACE2). The ACE2 is the host receptor of a protein known to have the highest expression in most tissues but can also bind to the SARS-CoV-2 spike protein. The inhibition of the receptions by active compounds of natural ingredients may result in effective treatment against corona virus infection. Ligands or active compounds that can inhibit the action of the SARS-CoV-2 protease also play a role in ACE2 inhibition. This work function plays a role in reducing the work of the SAR-CoV-2 host receptor [22–26].

In this study, we performed *in silico* analysis of the sixty active compounds contained within *Z. officinale* against the main protease COVID-19, PDB ID 6LU7 SARS-CoV-2. The binding of the active compounds of natural ingredients to this viral protein may inhibit viral replication and transcription [27–31].

We hypothesis that the active compounds contained in *Z. officinale* can bind effectively with the main protease COVID-19. This bond can potentially act as agent against COVID-19. The computational prediction results may provide futher information on the ability of active compounds to accelerate the healing of COVID-19, given that *Z. officinale* is used as a therapeutic agent against COVID-19.

2 Materials and Methods

The research was initiated by collecting various data on the active chemical compound within *Z. officinale* from various published papers. About 60 of the most chemically dominant active compounds present in *Z. officinale* were obtained [6, 9, 15–21]. These sixty compounds were used as ligands for molecular docking of the SARS-CoV-2 PDB ID 6LU7 target protein. The data on commercial antiviral drugs were taken from several previously conducted studies [32–34]. The structure of the active compound in *Z. officinale* and the commercial antiviral drugs were made in 2D and 3D using ChemDraw12.0.

The structure of the COVID-19 protein used was downloaded from the Protein Data Bank (PDB ID 6LU7 SARS-CoV-2, https://www.rcsb.org/structure/6LU7). External validation and redocking analysis using native ligands were performed. The grid box was center on x, y, and z coordinates, x = -11.683, y = 14.686, z = 65.363, a box of 40 40 40 A˚ with a grid spacing of 0.375 A˚ was formed. The protein was used as a COVID-19 macromolecule model and processed using the AutoDock4.2 software program.

3 Results

Molecular docking studies of the chemical constituents of *Z. officinale* using viral proteins as receptor have been carried out. The viral protein used is 6LU7, the crystal structure of the main protease COVID-19. In this study, *in silico* testing was carried out on 60 chemical compounds reported to be contained in *Z. officinale*. Chemical compounds that have known antiviral activity were included as positive controls. In this study, the interaction between the active compound in *Z. officinale* and the main protease COVID-19 will be studied. If the active compound *Z. officinale* can bind to the main protease COVID-19, it will be predicted to be active as an antiviral SAR-CoV-2 with a small value of free energy and a small affinity value. Table 1 shows the constituents of chemical compounds in *Z. officinale.*

Table 1. The chemical constituents *Z. officinale* Roscoe and its specification

No	Compound	Formula	References
1	Adenin	$C_5H_5N_5$	[15]
2	6-Gingerol	$C_{17}H_{26}O_4$	[18, 19]
3	8 Gingerol	$C_{19}H_{30}O_4$	[15, 19]
4	10 Gingerol	$C_{21}H_{34}O_4$	[15, 19]
5	6-Paradol	$C_{17}H_{26}O_3$	[19]
6	8-Paradol	$C_{19}H_{30}O_3$	[15, 19]
7	10-Paradol	$C_{21}H_{34}O_3$	[15, 19]
8	Scopoletin	$C_{10}H_8O_4$	[15]
9	6 Shogaol	$C_{17}H_{24}O_3$	[16, 18, 19]
10	10 Shogaol	$C_{21}H_{32}O_3$	[15, 19]
11	6 Dehydroshogaol	$C_{17}H_{22}O_3$	[21]
12	Zingerone	$C_{11}H_{14}O_3$	[19, 20]
13	Zingiberene	$C_{15}H_{24}$	[6, 17]
14	1,8 Cineole	$C_{10}H_{18}O$	[6, 9]
15	α Curcumene	$C_{15}H_{22}$	[6, 9, 17]
16	α Farnesene	$C_{15}H_{24}$	[18]

(*continued*)

Table 1. (*continued*)

No	Compound	Formula	References
17	β Farnesene	$C_{15}H_{24}$	[6]
18	Farnesol 3	$C_{15}H_{26}O$	[18]
19	γ Cadinene	$C_{15}H_{24}$	[6]
20	β-Seiqu-phellandrene	$C_{15}H_{24}$	[6]
21	α Phellandrene	$C_{10}H_{16}$	[6, 9]
22	Nerolidol	$C_{15}H_{26}O$	[6]
23	Neral	$C_{10}H_{16}O$	[6, 9]
24	Nerolidol acetate	$C_{17}H_{28}O_2$	[18]
25	Nerolidyl propionate	$C_{18}H_{30}O_2$	[18]
26	Guaiol	$C_{15}H_{26}O$	[18]
27	β Bisabolol	$C_{15}H_{26}O$	[18]
28	β Bisabolene	$C_{15}H_{24}$	[6, 9]
29	δ Tocopherol	$C_{27}H_{46}O_2$	[18]
30	Ethyl butanoate	$C_6H_{12}O_2$	[6]
31	α Pinene	$C_{10}H_{16}$	[6, 9, 17]
32	β Pinene	$C_{10}H_{16}$	[6]
33	Camphene	$C_{10}H_{16}$	[6]
34	Terpinolene	$C_{10}H_{16}$	[6, 9]
35	Terpinen-4-ol	$C_{10}H_{18}O$	[6, 9, 17]
36	Octanal	$C_8H_{16}O$	[6]
37	β Thujene	$C_{10}H_{16}$	[6, 9]
38	β Myrcene	$C_{10}H_{16}$	[6]
39	β Linolool	$C_{10}H_{18}O$	[6]
40	Endoborneol	$C_{10}H_{18}O$	[6]
41	Verbenone	$C_{10}H_{14}O$	[6]
42	Capsaicin	$C_{17}H_{27}NO_3$	[18]
43	Geraniol	$C_{10}H_{18}O$	[6]
44	Geranial	$C_{10}H_{16}O$	[6]
45	α-Copaene	$C_{15}H_{24}$	[6, 9]
46	α -Cedrene	$C_{15}H_{24}$	[6, 9]
47	α Gurjunene	$C_{15}H_{24}$	[6, 9]
48	α Bergamotene	$C_{15}H_{24}$	[6, 9]
49	Aromadrendene	$C_{15}H_{24}$	[6]

(*continued*)

Table 1. (*continued*)

No	Compound	Formula	References
50	Germacrene D	$C_{15}H_{24}$	[6]
51	Germacrone	$C_{15}H_{22}O$	[6]
52	γ Muurolene	$C_{15}H_{24}$	[18]
53	Thiiofenchone	$C_{10}H_{16}S$	[6, 9]
54	Veridiflorol	$C_{15}H_{26}O$	[18]
55	Methyl linoleate	$C_{19}H_{34}O_2$	[18]
56	Lariciresinol	$C_{20}H_{24}O_6$	[18]
57	Matairesinol	$C_{20}H_{22}O_6$	[18]
58	Carveol	$C_{10}H_{16}O$	[18]
59	Decalin, 1-methoxymethyl	$C_{12}H_{22}O$	[18]
60	2,5 dibutylfuran	$C_{12}H_{20}O$	[18]
61	Hidroxyichloroquinine	$C_{18}H_{26}ClN_3O$	[32–34]
62	Lopinavir	$C_{37}H_{48}N_6O_5S_2$	[32–34]
63	Nelfinavir	$C_{32}H_{45}N_3O_4S$	[32–34]
64	Remdesivir	$C_{27}H_{35}N_6O_8P$	[32–34]
65	Ritonavir	$C_{37}H_{48}N_6O_5S_2$	[32–34]

We simulated molecular docking of the active compounds of *Z. officinale* to the main protease COVID-19. The results of molecular docking processing can be seen in Table 2 which shows the interaction between active compounds of *Z. officinale* and amino acid residues. The interaction between active compounds and the active site of the main protease COVID-19, 6LU7 protein determines the potential of the active compound as seen from the value of free energy produced and its affinity value. The protein used in molecular docking is a protein downloaded from a protein data bank with the code PDB ID 6LU7. This protein is found in COVID-19 and thus presented to the protein data bank database. Figure 1 describes the docking results of the main protease COVID-19, 6LU7 protein by active compounds present in *Z. officinale*. The picture showed the relationship of the active compound *Z. officinale* with the the main protease COVID-19 in its active protein site. The active compound in *Z. officinale* provides moderate and good anti-COVID-19 activity.

Table 2. Molecular Docking results of inhibitory potential of the Covid-19 of the chemical constituents *Zingiber officinale* Roscoe

No	Compounds	ΔG (kcal/mol)	Ki (μM)	Interaction with amino acid
1	Adenin	-4.87	269.13	Asn142 Phe140 Gly166 Met165 Leu4 His163
2	6-Gingerol	-6.35	22.03	Asn142 Phe140 Gly166 Leu4 His163 Leu141 Cys145 Gly143 Thr25 Thr26
3	8 Gingerol	-6.33	22.87	Asn142 Glu166 Leu4 His163 Leu141 Cys145 Gly143 Thr25 Thr26 Ser144 Gly143 Leu27 Met165
4	10 Gingerol	-6.15	31.04	Asn142 Phe140 Gly166 Leu4 His163 Leu141 Cys145 Gly143 Thr26 His41 Ser144 Leu27
5	6-Paradol	-6.45	18.77	Asn142 Phe140 Glu166 Leu4 His163 Leu27 Cys145 Gly143 Thr25 His41 Ser144 Met49 Met165
6	8-Paradol	-6.47	11.54	Asn142 Phe140 Gly143 Leu4 His163 Leu141 Cys145 Glu166 His41 His172 Thr25 Thr26
7	10-Paradol	-6.01	39.44	Asn142 Phe140 Gly143 Leu4 His41 Leu141 Cys145 Glu166 Ser144 Leu27 Thr25 Thr26
8	Scopoletin	-6.47	18.06	Asn142 Gly143 Leu4 His163 His172 Leu141 Cys145 Glu166 Ser144
9	6 Shogaol	-6.65	13.27	Phe140 Gly143 Leu4 His163 Leu141 Cys145 Glu166 His141 Thr25 Leu27 Ser144 Met165
10	10 Shogaol	-7.12	6.04	His41 His163 His172 Cys145 Met165 Glu166
11	6 Dehydroshogaol	-7.21	5.16	His41 His163 His172 Cys145 Met165 Gly143 Phe140 Leu141 Ser144
12	Zingerone	-5.77	58.95	Phe140 Gly143 Leu4 His163 Leu141 Cys145 Glu166 His172 Ser144
13	Zingiberene	-8.11	1.13	His41 His164 Phe181 Cys145 Gly143 Leu141 Met49 Met165 Leu27

(*continued*)

Table 2. (*continued*)

No	Compounds	ΔG (kcal/mol)	Ki (μM)	Interaction with amino acid
14	1,8 Cineole	-6.75	11.36	Phe140 Leu4 His163 Leu141 Cys145 Glu166 His172 Ser144 Met165 Val3
15	α Curcumene	-7.37	3.95	His41 His163 His172 Cys145 Met165
16	α Farnesene	-7.07	6.59	His41 His164 Met49 Met165 Leu167 Pro168
17	β Farnesene	-6.66	13.03	Asn142 Phe140 Glu166 Leu4 His163 Leu27 Cys145 Gly143 His172 Leu141 Met165 Ser144 Thr25 Thr26
18	Farnesol 3	-6.41	19.93	Phe140 Leu4 His163 Leu141 Cys145 Glu166 His172 Gly143 Leu27 Met165 Thr26 Val3
19	γ Cadinene	-7.22	5.09	His41 His163 Cys145 Met165 Gly143
20	β Seiqu-phellandrene	-7.70	2.25	His41 His163 Cys145 Met165 Met49 His172
21	α Phellandrene	-6.36	21.85	Asn142 Phe140 Glu166 Leu4 His163 Cys145 Gly143 Leu141 His172 Ser144
22	Nerolidol	-6.77	10.83	Asn142 Phe140 Glu166 Leu4 His163 Cys145 Gly143 Leu141 His41 Ser144 Leu27 Thr26 Val3 Met165
23	Neral	-5.54	86.75	Asn142 Phe140 Glu166 Leu4 His163 Cys145 Gly143 Leu141 Ser144 Val3 Met165
24	Nerolidol acetate	-6.74	11.45	Asn142 Glu166 Leu4 His163 Cys145 Gly143 Leu141 His41 His164 Met165 Thr25 Val3 Met49
25	Nerolidyl propionate	-6.75	11.34	Asn142 Phe140 Glu166 Leu4 His163 Cys145 Gly143 Leu27 Ser144 Val3 His41 Thr25
26	Guaiol	-6.05	36.91	Asn142 Leu4 His41 Cys145 Gly143 Leu27 Thr25

(*continued*)

Table 2. (*continued*)

No	Compounds	ΔG (kcal/mol)	Ki (μM)	Interaction with amino acid
27	β Bisabolol	-7.81	1.88	His41 Met165 Glu166 Leu167 Pro168
28	β Bisabolene	-7.86	1.72	His41 His163 His164 Cys145 Met49 Phe181 Met165
29	δ Tocopherol	-7.54	2.96	His41 His163 Cys145 Met165 Thr26
30	Ethyl butanoate	-3.80	1630	Phe140 Leu4 His172 Leu141 Cys145 Glu166 Gly143 Met165
31	α Pinene	-6.51	17.02	Phe140 Leu4 Leu141 Cys145 Glu166 Met165 Val3 Ser144
32	β Pinene	-6.53	16.38	Asn142 Phe140 Glu166 Leu4 His163 Cys145 Val3 Leu141 Ser144
33	Camphene	-6.43	19.42	Asn142 Phe140 Glu166 Leu4 His163 Val3 Leu141 Ser144 Met165
34	Terpinolene	-6.17	30.2	Asn142 Phe140 Glu166 Leu4 His163 His172 Cys145 Gly143
35	Terpinen-4-ol	-6.46	18.46	Asn142 Phe140 Glu166 Leu4 His163 His172 Cys145 Gly143 Val3 Ser144 Leu141
36	Octanal	-4.30	700.61	Glu166 Leu4 His163 Cys145 Gly143 Val3 Ser144 Leu141 Met165 Leu27
37	β Thujene	-5.96	43.11	Asn142 Phe140 Glu166 Leu4 His163 His172 Cys145 Gly143 Val3 Leu141 Met165
38	β Myrcene	-5.52	89.8	Phe140 Leu4 Leu141 Cys145 Met165 His41 His163 Leu27 Gly143
39	β Linolool	-5.73	63.42	Phe140 Leu4 Leu27 Cys145 Met165 His163 Gly143 Glu166 Val3
40	Endoborneol	-5.56	83.65	Asn142 Phe140 Glu166 Leu4 His163 His172 Val3 Leu141 Met165 Ser144

(*continued*)

Table 2. (*continued*)

No	Compounds	ΔG (kcal/mol)	Ki (μM)	Interaction with amino acid
41	Verbenone	-6.08	34.88	Asn142 Phe140 Glu166 Leu4 His163 His172 Val3 Leu141 Met165 Ser144 Cys145 Gly143
42	Capsaicin	-7.06	6.7	His41 His164 Cys145 Met165 Leu141
43	Geraniol	-5.71	65.28	Glu166 Leu4 His163 Cys145 Gly143 Leu141 Met165 Leu27 His172 His41
44	Geranial	-5.55	85.75	Asn142 Phe140 Glu166 Leu4 His163 His41 Leu141 Leu27 Met165 Cys145 Gly143 His172
45	α-Copaene	-6.74	11.5	Asn142 Leu4 Leu141 Met49 Cys145 Gly143 Ser144 Thr25
46	α -Cedrene	-6.40	20.28	Asn142 Leu4 Leu27 Met49 Cys145 Gly143 Thr25 Thr26 His41
47	α Gurjunene	-6.93	8.3	His41 Met49 Met165 Cys145
48	α Bergamotene	-7.87	1.7	His41 His163 Met49 Met165 Cys145
49	Aromadrendene	-6.19	29.03	Leu4 Leu27 Met49 Cys145 Gly143 Thr25 Thr26 His41
50	Germacrene D	-6.33	22.83	Asn142 Leu4 Leu27 Met49 Cys145 Gly143 Thr25 Thr26 Leu141
51	Germacrone	-6.05	37.06	Asn142 Leu4 His41 Cys145 Gly143 Met49
52	γ Muurolene	-6.76	11.15	Asn142 Leu4 Leu141 His41 Cys145 Gly143 Met49 Leu27 Ser144
53	Thiiofenchone	-6.22	27.82	Asn142 Phe140 Glu166 Leu4 His163 Leu141 Cys145 Val3 Ser144 Met165 His172
54	Veridiflorol	-6.06	36.28	Asn142 Leu4 His41 Cys145 Gly143 Leu27 Thr25 Thr26
55	Methyl linoleate	-6.15	31.15	Leu4 Leu27 Met49 Cys145 Gly143 Thr25 Thr26 His163 Glu166 Ser144 Leu141

(*continued*)

Table 2. (*continued*)

No	Compounds	ΔG (kcal/mol)	Ki (μM)	Interaction with amino acid
56	Lariciresinol	-8.20	0.97	Glu166 Cys145 Met165 Thr25 Thr26 Leu27
57	Matairesinol	-7.59	2.75	His41 His163 His164 Asn142 Phe140 Leu141 Cys145 Met49 Met165
58	Carveol	-6.30	24.24	Asn142 Phe140 Glu166 Leu4 His163 Leu141 Cys145 Gly143 His172
59	Decalin, 1-methoxymethyl	-6.51	16.77	Asn142 Phe140 Glu166 Leu4 His163 Leu141 Cys145 His172 Ser144 Val3
60	2,5 dibutylfuran	-6.07	35.47	Phe140 Leu27 Met165 Cys145 Gly143 Thr25 His163 Glu166 Ser144 Leu141 Val3 His172
61	Hydroxychloro quinin	-8,23	0.930	Leu4 Met49 Thr45 Ser144 Cys145 Leu27 Gly143 Thr25 Asn142 Leu141
62	Lopinavir	-5.56	0.083	Gln189 Met165 Leu4 Met49 Val3 Glu166 Ser46 Thr45 His163 Asn142 Cys145 Leu27 Gly143 Thr26 Thr25 Thr24
63	Nelfinavir	-8.79	0.360	Met49 His41 Cys145 Leu27 Gln189 Glu166 Phe140
64	Remdesivir	-6.81	0.01	Gln189 Glu166 His41 His163 Met49 Leu27 Leu141 Thr26 Asn142 Met165 Cys145
65	Ritonavir	-7.53	0.003	Glu166 Met165 Met49 His164 His41

4 Discussion

In this current study, 60 active compounds *Z. officinale* Roscoe were screened. Five commercial antiviral compounds were used as positive controls. The main protease enzyme (MPro) of SARS-CoV-2 can be considered as the key in virus production and its crystal structure is also available with excellent resolution. The presence of this enzyme receptor is a good initial receptor for conducting structure-based virtual screening studies to determine the best hits contained in *Z. officinale*. The computational simulation described any interaction present between the active compound and the SAR-CoV-2 amino acid residues. In the molecular docking simulation, the interaction of amino acids with active compounds very influential in producing free energy and affinity which play an important role in predicting the activity of the compound against in the host receptor. The

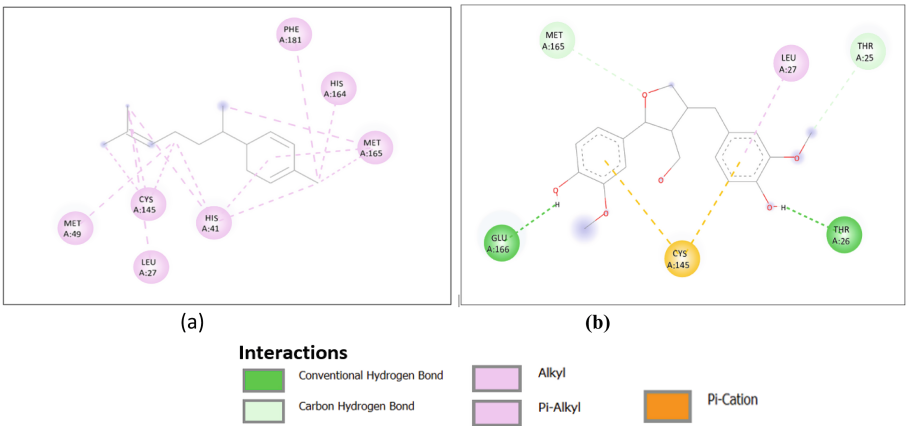

Fig. 1. Interaction active compound of *Z. officinale:* (a) Zingiberene and (b) Lariciresinol with amino acid residue of the main protease COVID-19

antiviral mechanism of SAR-CoV-2 can be understood from the interaction between the ligand and the amino acid residue. The results of molecular docking of 60 chemical compounds contained in *Z. officinale* showed that 2 chemical compounds, Zingiberene (**13**) and Lariciresinol (**56**) in *Z. officinale* had the highest activity. There were 13 compounds (**10**, **11**, **15**, **16**, **19**, **20**, **27**, **28**, **29, 42**, **47**, **48**, **57**) with moderate activity.

The model depicting the docking molecule shows that 60 compounds of *Z. officinale* have the ability to bind to areas affected by the main protease Covid-19. Compound Zingiberene (**13**) and compound Lariciresinol (**56**) have the best Gibbs energy of -8.11 and -8.20, which is almost equivalent to commercial antiviral drugs [32–34]. Zingiberene showed interaction with the amino acid residues Leu27, His41, Met49, Cys145, His164, Met165 and Phe181, having π interactions with Cys145 and His41. Meanwhile, Lariciresinol showed interaction with amino acid residues Thr25, Thr26, Leu27, Cys145, Met165 and Glu166. There are 2 conventional hydrogen bonds with Thr26 and Glu166, and 2 hydrogen bonds with Thr26 and Met165 and π cation interaction with Cys145. The binding interaction of Zingiberene and Lariciresinol with the main protease Covid-19 is shown in Fig. 1. The interaction of active compounds with Met49, Glu166 and Cys145 plays a vital role in inhibiting SAR-CoV-2. The interaction with the residual amino acids of methionine, glutamic acid and cysteine greatly affects the value of the free energy produced. The afore mentioned amino acids are the main structural amino acid of the SAR-CoV-2 receptors [35]. Other amino acid residues that are equally important in inhibiting the SAR-Cov-2 protease include; Leu27, His41, Met165, Gln189, Phe181, His164, Thr 25 and Thr26. Protease is a protein that can represent a target for inhibition of viral replication or transcription. Inhibition of this can cause various diseases. This host protease is one of the potential protein targets for therapy. Proteases are widely used in the treatment of viruses since viral replication generally occurs with the aid of proteases. Currently proteases are widely used in the development of antiviral therapy and as a target protein.

Docking results show chemical interactions Zingiberene and Lariciresinol of *Z. officinale* with SAR-CoV-2 amino acid residues, including Methionine49, Methionine165, Histidine41, Glutamic acid166, Leucine27, Histidine164, Histidine172, Phenylalanine140, Phenylalanine181, Threonine26, Threonine 25, Cysteine145, Serine144, Glysine143, Proline168, Leucine167 and Leucine141. Fifteen of the 60 analyze by the molecular docking test showed the ability to inhibit the COVID-19 protein. The molecular docking simulation showed that *Z. officinale* has activity against the SARS-CoV-2 6LU7 protein. The biological activity of potential active compounds in *Z. officinale* against SARS-CoV-2 and its associated mechanisms of action must be investigated further.

5 Conclusion

In this study, 60 active compounds Z. officinale Roscoe were filtered. In the docking molecular simulation, the interaction of amino acids with ligands/active compounds is very influential in producing free energy and affinity. These free energy and affinity values play an important role in predicting the activity of a ligand/compound in the host receptor. The antiviral mechanism of SAR-Cov-2 can be understood from the interaction between the ligand and the amino acid residue. The results of molecular docking of 60 chemical compounds contained in Z. officinale showed that there were 2 chemical compounds in Z. officinale (Zingiberene and Lariciresinol) which had the highest activity. The biological activity of potential active compounds in Z. officinale against SARS-CoV-2 and its associated mechanisms of action must be investigated further.

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