Bioactive Compounds from Purslane (Portulaca oleracea L.) and Star Anise (Illicium verum Hook) as SARS-CoV-2 Antiviral Agent via Dual Inhibitor Mechanism: In Silico Approach

Nur Sofiatul Aini¹, Viol Dhea Kharisma², Muhammad Hemawan Widyananda³,⁴, Ahmad Affan Ali Murtadjo⁵, Rayyadon Taufiq Probojati⁶, Dora Dayu Rahma Turista⁶, Muhammad Badrul Tamam⁷, Vikash Jakholma⁷, Dony Novaliendry⁸, Riso Sari Mandell⁹,¹⁰, Budhi Oktavia¹⁰,¹¹, Muhammad Thoriq Albani¹²,¹³, Saddam Al Aziz¹⁴,¹⁵, Muhammad Raffi Ghifari¹⁶,¹⁷, Okta Suryanti¹⁸, Putri Azhari¹⁹,²⁰, Muhammad Arya Ghifari²¹,²², Devi Purnamasari²³,²⁴, Agariadne Dwiringgo Sama³,²⁵, Mirella Fonda Maahury²⁶, ANM Ansori²⁷, Rahadian Zainul²⁸,²⁹

¹Faculty of Mathematics and Natural Sciences, State University of Surabaya, Surabaya, Indonesia.
²Division of Molecular Biology and Genetics, Gernatasi Bioiologi Indonesia Foundation, Greek, Indonesia.
³Department of Biology, Faculty of Mathematics and Natural Sciences, Brawijaya University, Malang, Indonesia.
⁴Faculty of Agriculture, Universitas Kediri, Kediri, Indonesia.
⁵Biokimia Eksperimen Department, Faculty of Teacher Training and Education, Muhammadiyah University, Solo, Indonesia.
⁶Department of Biology, Faculty of Sciences and Technology, Universitas Muhammadiyah Lampongan, Lampongan, Indonesia.
⁷Utarakhamal Institute of Pharmaceutical Sciences, Uttarakhamal University, Dehradun, India.
⁸Center for Advanced Material Processing, Artificial Intelligence, and Biophysics Informatics (CAMP-BIOTICS), Universitas Negeri Padang, Padang, Indonesia.
⁹Study Program of Informatics, Faculty of Engineering, Universitas Negeri Padang, Padang, Indonesia.
¹⁰Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Negeri Padang, Padang, Indonesia.
¹¹Department of Informatics and Computer Engineering, Faculty of Mathematics and Natural Sciences, Universitas Negeri Padang, Padang, Indonesia.
¹²Department of Agriculture Technology, Faculty of Agriculture Technology, Andalas University, Padang, Indonesia.
¹³Department of Radiology Engineering, Universitas Awan Bros, Pekanbaru, Indonesia.
¹⁴Department of Informatics and Computer Engineering, Faculty of Engineering, Universitas Negeri Padang, Padang, Indonesia.
¹⁵Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Pattimura, Ambon, Indonesia.
¹⁶Professor Hadim Foundation, Surabaya, Indonesia.

Correspondence
Rahadian Zainul
Center for Advanced Material Processing, Artificial Intelligence, and Biophysics Informatics (CAMP-BIOTICS), Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Negeri Padang, Padang, Indonesia.
E-mail: rahadianzmsiphd@fmipa.unp.ac.id

ABSTRACT
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes the COVID-19 pandemic that infects humans and attacks the body’s immune system. The purpose of the study was to identify the potential of bioactive compounds in purslane (Portulaca oleracea L.) and star anise (Illicium verum Hook) via a dual inhibitor mechanism against SARS-CoV-2 proteases with an in silico approach. The samples were obtained from PubChem and RSCB PDB. Antivirus probability prediction was performed on PASS Online. Virtual screening was performed with PyRx via molecular docking. Visualization was used by PyMol and Discovery Studio. Compounds with the best antiviral potential are indicated by the low binding affinity value to the target proteins, namely SARS-CoV-2 TMPRSS2 and PLpro. The results showed that purslane luteolin has the best antiviral potential. However, further studies are required to validate this computational prediction.

Key words: SARS-CoV-2, Portulaca oleracea L., Illicium verum Hook, In silico, Antiviral agent.

INTRODUCTION
Coronavirus disease 2019 or the COVID-19 pandemic caused by severe acute respiratory syndrome (SARS-CoV-2) causes numerous economic and health losses.² According to the most recent data, over 530 million cases have been reported worldwide. Furthermore, there are 6 million cases of infection and over 150 thousand deaths in Indonesia.³ So far, three coronavirus outbreaks have been reported in the 21st century, namely SARS-CoV (2002-2003), MERS-CoV (2012), and SARS-CoV-2 (2020-present).¹ Humans can be infected by four other coronaviruses including HCoV-229E, HCoV-HKU1, HCoV-NL63, and HCoV-OC43 which cause mild respiratory illnesses such as common fever.¹⁷ SARS-CoV-2 shares 80% genomic similarity with the SARS-CoV virus.¹⁸ SARS-CoV-2 has a genome length of 29,903 bp and ssRNA as genetic material.¹⁹ This virus has 4 structural proteins: envelope protein (E), membrane glycoprotein (M), nucleocapsid phosphoprotein (N), and spike glycoprotein (S).²⁰ In addition, there are two proteases that play an important role in this viral infection such as transmembrane protease serine 2 (TMPRSS2) and papain-like protease (PLpro).²¹,²² TMPRSS2 plays a role in viral entry along with furin in the activation of angiotensin converting enzyme 2 (ACE2).²³ Meanwhile, PLpro aids in viral protein maturation and folding as well as the suppression of immune response in host cells.²⁴ Indonesia is a megabiodiversity country with 7500 medicinal plant species either native or introduced, wild or cultivated.²⁵ Some such plants are used as folk remedies for a long time such as purslane (Portulaca oleracea L.) and star anise (Illicium verum Hook). Purslane is a weed member of the Portulacaceae.²⁶ The plant is distributed in tropical and subtropical regions around the world and native to South America and Africa.²⁷ Meanwhile, star anise is a member of the Magnoliaceae which is found in the tropics and subtropics. The plant is native to China and Vietnam.²⁸ Several studies have shown the potential of purslane as an antiviral for influenza A (IAV) and herpes simplex type 2 (HSV-2).²⁹,³⁰ Meanwhile, star anise has antiviral potential against influenza A and B as well as herpes simplex type 1 and 2.³¹,³² However, the anti-SARS-CoV-2 potential of purslane and star anise bioactive compounds is unknown. Therefore, this study aims to identify the potential of purslane and star anise bioactive compounds using in silico approach via the mechanism of two inhibitors against SARS-CoV-2 proteases.

MATERIALS AND METHODS
Sample preparation
The bioactive compounds found in purslane are apigenin, isorhamnetin, and luteolin. Meanwhile, star anise has shikimic acid, illicinone, and illicinone A. Data were provided by PubChem. Furthermore, non-structural target protein databases TMPRSS2 and PLpro were obtained from RSCB PDB. Antiviral probability prediction
Prediction of the probability of bioactive compounds is carried out with the PASS Online web server.

Cite this article: Aini NS, Kharisma VD, Widyanaanda MH, Murtadjo AAA, Probojati RT, Turista DDR, et al. Bioactive Compounds from Purslane (Portulaca oleracea L.) and Star Anise (Illicium verum Hook) as SARS-CoV-2 Antiviral Agent via Dual Inhibitor Mechanism: In Silico Approach. Pharmacogn J. 2022; 14(4): 352-357.
 she extraction of bioactive compounds from Purslane (Portulaca oleracea L.) and Star Anise (Illicium verum Hook) as SARS-CoV-2 Antiviral Agent via Dual Inhibitor Mechanism: In Silico Approach

**Figure 1:** Visualization of ligand and targeted protein. Bioactive compounds from: A) purslane, B) star anise, and C) targeted proteins on the SARS-CoV-2.

**Figure 2:** The binding visualization of luteolin on the targeted proteins: A) TMPRSS2 and B) PLpro.
Predictions are expressed as potential antivirals if the activity probability value (Pa) is greater than 0.3.12

Virtual screening

Virtual screening was performed by molecular docking between the selected bioactive compounds and the targeted proteins TMPRSS2 and PLpro. Molecular docking was performed using PyRx software.25 The molecule that has the most negative results is the molecule that has the most potential as an antiviral in both target proteins. The bond between the ligand and the target protein is expressed in the bond affinity value (kcal/mol).26

Interaction and visualization

Compounds with the highest negative binding affinity values were then analyzed to determine the position and interaction of their chemical bonds using PyMol and Biovia Discovery Studio.27

RESULT AND DISCUSSION

Online PASS results revealed that drug candidate compounds performed well and were computationally proven if the Pa score was higher than the Pi score as well as the Pa score >0.3. However, in vivo and in vitro analysis are required to confirm the antiviral potential of bioactive compounds.23 However, four compounds have a Pa value of <0.3 and the other two do not (Table 1).

The results of molecular docking are expressed in binding affinity indicating the energy of the stabilized bond formed between the ligand-receptor complexes. The degree of binding affinity influences biological activity when binding to proteins.24 In this study, biological activity was demonstrated by inhibiting SARS-CoV-2 and body cells through interaction of bioactive compounds and target proteins.29 The bond affinity value that used in this study is the smallest because it indicates the presence of additional stability and higher inhibition activity performed by the ligand towards the protein target.30,31 The presence of bond types, amino acids on the active side, and amino acid residues on the ligands affects the affinity of the bond between the ligands and receptors.31 The more hydrogen bonds, the more stable the ligand-protein interaction.24 According to molecular docking simulations, luteolin has the compound with the most negative energy of two target proteins and has the potential to be a potential antiviral two inhibitors (Table 2).

### Table 1: Antiviral probability of selected compounds from purslane and star anise.

| Plant            | Compound       | Antiviral Probability |
|------------------|----------------|-----------------------|
| Purslane (P. oleracea L.) | Apigenin | 0.209 0.089 |
|                  | Isohamnetin   | 0.204 0.092 |
|                  | Luteolin      | 0.220 0.080 |
| Star anise (I. verum Hook) | Shikimic acid | 0.217 0.082 |
|                  | Illicinole     | - - |
|                  | Illicinone A   | - - |

### Table 2: Binding affinity (kcal/mol) of ligand protein complexes.

| Plant            | Compound       | Binding Affinity (kcal/mol) |
|------------------|----------------|-----------------------------|
|                  | TMPRSS2        | PLpro                       |
| Purslane (P. oleracea L.) | Nirmatrelvir | -6.4 -7 |
|                  | Apigenin       | -7 -8                        |
|                  | Isohamnetin    | -7.1 -8.5                   |
|                  | Luteolin       | -7.3 -8.5                   |
| Star anise (I. verum Hook) | Shikimic acid | -5.6 -5.2 |
|                  | Illicinole     | -5.9 -6.2                   |
|                  | Illicinone A   | -5.6 -7                      |

TMPRSS2 has a catalytic region composed of triads of amino acid residues His296, Asp345, and Ser461.13 This position is targeted by drug candidate bioactive compounds to inhibit SARS-CoV-2 entries through human cell membranes. Luteolin may interact with Ser436 through hydrogen bonds and with His296 through Pi-Pi T shaped bonds. The negative binding energy generated by hydrogen bonds aids stabilizes the binding between luteolin and TMPRSS2.24 Pi-pi T shaped interaction is the interaction of electron pi clouds between two aromatic groups in the form of T.25 The presence of pi-pi T shaped interaction affects the protein stability and flexibility and is important in drug intercalation and supramolecular chemistry.26,28

PLpro has catalytic triads and important catalytic residues. The catalytic triad consists of Sys111Ser, His272, and Asp286. Catalytic residues in these non-structural proteins include Trp93, Trp106, Asp108, and Asn109.27 During the molecular docking process, luteolin interacts with Trp106 and Trp259 residues through hydrogen bonds; Ala107 via Pi-alkyl; and Asp108, Lys217; and Glu307 via Pi-anion. The presence of hydrogen bonds aids stabilization of bonds during screening via molecular docking.27 Furthermore, the Pi-alkyl interaction is an interaction of the aromatic group electron cloud with other alkyl group electron clouds. While the Pi-anion interaction is a contact between the aromatic system of the electron (pi- acid) and an anion.28 Some amino acid residues have van der Waals bonds to ligands shown in light green color. This weak bond affects the binding affinity between the ligand and protein complex affecting the inhibition of viral entries, maturation, and protein folding.29,30 The existence of such non-covalent interactions is preferred in molecular docking because it plays a role in catalytic processes and stabilization.30,41

Research on massive SARS-CoV-2 has been conducted in recent years. Several medicinal plants were tested for antiviral activity against this virus. TMPRSS2 in human cell membranes and PLpro SARS-CoV-2 are two examples of such studies. In silico studies involving herbal plants reported that niazinir, quercetin, and moringynene from moringa (Moringa oleifera) and curcumin from several Indonesian herbal products have potential as TMPRSS2 inhibitors.42,43 Meanwhile, magostin compound in mangooseen (Garcinia mangostana) and quercetin in several dietary plants have the potential to be an in silico inhibitor of PLpro.14,45 The entire in silico research aims to develop SARS-CoV-2 antiviral candidates. However, further in vivo and in vitro analyses are required to confirmation of potency.46-51

CONCLUSION

The combination of purslane (Portulaca oleracea L.) and star anise (Illicium verum Hook) bioactive compounds has the potential to be an antiviral of SARS-CoV-2. Luteolin is a purslane bioactive compound with the lowest binding energy to SARS-CoV-2 TMPRSS2 and PLpro. However, more research is required to support the results of this study.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest.

REFERENCES

1. Ansori ANM, Kharisma VD, Muttaqin SS, Antonius Y, Parikesit AA. Genetic variant of SARS-CoV-2 isolates in Indonesia: Spike glycoprotein gene. J Pure Applied Microbiol. 2020;14(1):971-8.
2. Fahmi M, Kharisma VD, Ansori ANM, Ito M. Retrieval and investigation of data on SARS-CoV-2 and COVID-19 using bioinformatics approach. Adv Exp Med Biol. 2021;1318:839-57.
3. Ansori ANM, Kharisma VD, Fadholly A, Tacharina MR, Antonius Y, Parikesit AA. Severe Acute Respiratory Syndrome Coronavirus-2 Emergence and Its Treatment with Alternative Medicines: A Review. R J Pharma Technol. 2021;14(10):5551-7.
4. Kharisma VD, Ansori AN, Probojati RT, Turista DD, Antonius Y. Concept of SARS-CoV-2 Vaccine Design to Fight COVID-19 Pandemic: A Review Insight. Indian J Forensic Med Toxicol. 2021;15(4):2797-803.

5. Turista DDR, Islamy A, Kharisma VD, Ansori ANM. Distribution of COVID-19 and phylogenetic tree construction of SARS-CoV-2 in Indonesia. J Pure Applied Microbiol. 2020;14:1035-42.

6. Kharisma VD, Ansori ANM. Construction of epitope-based peptide vaccine against SARS-CoV-2: Immunoinformatics study. J Pure Appl Microbiol. 2020;14(11):999-1005.

7. Ansori ANM, Antonius Y. A phylogenetic analysis of Indonesian SARS-CoV-2 isolates from March to December 2020: Compared with Delta and Mu variant. Jurnal Teknologi Laboratorium. 2022;11(1).

8. Xu J, Zhao S, Teng T, Abdalla AE, Zhu W, Xie L, et al. Systematic comparison of two animal-to-human transmitted human Coronavirus: SARS-CoV-2 and SARS-CoV. Viruses. 2020;12(11):244.

9. Dibha AF, Wahyuningisih S, Kharisma VD, Ansori AN, Widyananda MH, Parikesit AA, et al. Biological activity of kencur (Kaempferia galanga L.) against SARS-CoV-2 main protease: In silico study. Int J Health Sci. 2022;6(1):468-80.

10. Hafidzhah MA, Wijaya RM, Probojati RT, Kharisma VD, Ansori ANM, Parikesit AA. Potential vaccine targets for COVID-19 and phylogenetic analysis based on the nucleocapsid phosphoprotein of Indonesian SARS-CoV-2 isolates. Indonesian J Pharm. 2021;32(2):328-37.

11. Shereen MA, Khan S, Kazmi A, Bashir N, Siddique R. COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. J Adv Res. 2020;24:91-8.

12. Ansori ANM, Kharisma VD, Parikesit AA, Dian FA, Probojati RT, Rebezo M, et al. Bioactive compounds from mangosteen (Garcinia mangostana L.) as an antiviral agent via individual inhibitor mechanism against SARS-CoV-2: An in-silico approach. Pharmacogn J. 2022;14(1):85-90.

13. Hoffman M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell. 2020;2(1):62.

14. Padmi H, Kharisma VD, Ansori ANM, Sibero MT, Widyananda MH, Ullah ME, et al. Macrolactone bioactive compounds for the potential antiviral of SARS-CoV-2: An in-silico study. J Pure Appl Microbiol. 2022;2022:7470.

15. Nogara PA, Omage FB, Bolzan GR, Delgado CP, Aschner M, Orion L, et al. In silico studies on the interaction between Mpro and PLpro from SARS-CoV-2 and ebolien, its metabolites and derivatives. Mol Inform. 2021;40(8):e2100020.

16. Ansori ANM, Kusala MKJ, Iravan H, Putri N, Fadholly A, Proboningrat A, et al. Citrus reticulate extract as biocides to control Aedes aegypti, the vector of dengue. Biosci Res. 2018;28(6):1661-5.

17. Ocampo G, Columbus JT. Molecular phylogenetics, historical biogeography, and chromosome number evolution of Portulaca (Portulacaaceae). Mol Phylogenet Evol. 2012;63(1):97-112.

18. Kumar A, Sreedharan S, Kashyap AK, Singh P, Ramchay N. A review on bioactive phytochemicals, ethnomedical and pharmacological importance of purslane (Portulaca oleracea L.). Heilonyon. 2021;8(1):E08669.

19. Allahverdivey AM, Bagirova M, Yaman S, Koc RC, Abamor ES, Ates SC, et al. Development of new antitherpetic drugs based on plant compounds. In: MK Rai & KV Kon (Eds.), Fighting multidrug resistance with herbal extracts, essential oils and their components (245-259). Elsevier. 2013.

20. Dong C-X, Hayashi K, Lee J-B, Hayashi T. Characterization of structures and antiviral effects of polysaccharides from Portulaca oleracea L. Chem Pharm Bull. 2010;58(4):507-510.

21. Li Y-H, Lai C-Y, Su M-C, Cheng J-C, Chang Y-S. Antiviral activity of Portulaca oleracea L. against influenza A viruses. J Ethnopharmacol. 2019;241:112013.

22. Koch C, Reichling J, Schneeie J, Schnitzler P. Inhibitory effect of essential oils against herpes simplex virus type 2. Phytomedicine. 2008;15(1-2):71-8.

23. Kharisma VD, Probojati RT, Mustadi AAA, Ansori ANM, Antonius Y, Tamam MB. Revealing potency of bioactive compounds as inhibitor of dengue virus (DENVI NS2b/NS3 protease from sweet potato (Ipomoea batatas L.) leaves. Indian J Forensic Med Toxicol. 2021;15(1):1627-32.

24. Patra JK, Das G, Bose S, Banerjee S, Vishnuprasad CN, Rodriguez-Torres MP, et al. Star anise (Illicium verum): Chemical compounds, antiviral properties, and clinical relevance. Phytotherapy Res. 2020;2020:1-20.

25. Antonius Y, Utomo DH, Wido. Identification of potential biomarkers in nasopharyngeal carcinoma based on protein interaction analysis. Int J Bioinform Res Appl. 2017;13(4):376-88.

26. Kharisma VD, Agatha A, Ansori ANM, Widyananda MH, Rizky WC, Dings TGA, et al. Herbal combination from Monigna oleifera Lam. and Curcuma longa L. as SARS-CoV-2 antiviral via dual inhibitor pathway: A viroinformatics approach. J Pharm Pharmacogn Res. 2022;10(1):138-46.

27. Wijaya RM, Hafidzhah MA, Kharisma VD, Ansori ANM, Parikesit AA. COVID-19 in silico drug with Zinger officinalis natural product compound library targeting the Mpro protein. Makara J Sci. 2021;25(3):162-71.

28. Onkgo J, Setiaawan JV, Feronytha AG, Juliana A, Effrain A, Wahjudi M, et al. In-silico screening of inhibitor on protein epidermal growth factor receptor (EGFR). IOP Conference Series: Earth and Environmental Science. 2022;1041:012075.

29. Amin SA, Banerjee S, Ghosh K, Gayen S, Jha T. Protease targeted COVID-19 drug discovery and its challenges: Insight into viral main protease (Mpro) and papain-like protease (PLpro) inhibitors. Bioorganic Med Chem. 2021;29:115860.

30. Prahananti C, Nugraha AP, Kharisma VD, Ansori ANM, Ridwan RD, Putri TPS, et al. A bioinformatics approach of hydroxyapatite and polyethylene/methacrylate composite exploration as dental implant biomaterial. J Pharm Pharmacogn Res. 2021;(9):746-54.

31. Listiyan R, Kharisma VD, Ansori ANM, Widyananda MH, Probojati RT, Mustadi AAA, et al. In silico phytochemical compounds screening of Allium sativum targeting the Mpro of SARS-CoV-2. Pharmacogn J. 2022;14(3):604-9.

32. Widyananda MH, Pratama SK, Samoedra RS, Sari FN, Kharisma VD, Ansori ANM, et al. Molecular docking study of sea urchin (Arbacia lixula) peptides as multi-target inhibitor for non-small cell lung cancer (NSCLC) associated proteins. J Pharm Pharmacogn Res. 2021;9(4):484-96.

33. Thunders M, Delshunt B. Gene of the month: TMPRSS2 (transmembrane serine protease 2). J Clin Pathol. 2020;73(12):773-6.

34. Kharisma VD, Widyananda MH, Ansori ANM, Nege AS, Nwe SW, Nugraha AP. Tea catechin as antiviral agent via apoptosis agonist and triple inhibitor mechanism against HIV-1 infection: A bioinformatics approach. J Pharm Pharmacogn Res. 2021;9(4):435-45.

35. Wang YZ, Wu AX. π-π interaction in aromatic supramolecular system. Chinese J Organic Chem. 2008;28(6):997-1011.

36. Yang CY, Phillips JG, Stuckey JA, Bai L, Sun H, Delproposto J, et al. Revealing potency of bioactive compounds as potential vaccine targets for COVID-19 and phylogenetic tree construction of SARS-CoV-2 in Indonesia. J Pure Applied Microbiol. 2020;14(4):2797-803.

37. Li Y-H, Lai C-Y, Su M-C, Cheng J-C, Chang Y-S. Antiviral activity of Portulaca oleracea L. against influenza A viruses. J Ethnopharmacol. 2019;241:112013.

38. Koch C, Reichling J, Schneeie J, Schnitzler P. Inhibitory effect of essential oils against herpes simplex virus type 2. Phytomedicine. 2008;15(1-2):71-8.

39. Kharisma VD, Probojati RT, Mustadi AAA, Ansori ANM, Antonius Y, Tamam MB. Revealing potency of bioactive compounds as inhibitor of dengue virus (DENVI NS2b/NS3 protease from sweet potato (Ipomoea batatas L.) leaves. Indian J Forensic Med Toxicol. 2021;15(1):1627-32.

40. Patra JK, Das G, Bose S, Banerjee S, Vishnuprasad CN, Rodriguez-Torres MP, et al. Star anise (Illicium verum): Chemical compounds, antiviral properties, and clinical relevance. Phytotherapy Res. 2020;2020:1-20.
Aini NS, et al.: Bioactive Compounds from Purslane (Portulaca oleracea L.) and Star Anise (Illicium verum Hook) as SARS-CoV-2 Antiviral Agent via Dual Inhibitor Mechanism: In Silico Approach

37. Gao X, Qin B, Chen P, Zhu K, Hou P, Wojdyla JA, et al. Crystal structure of SARS-CoV-2 papain-like protease. Acta Pharmaceutica Sinica B. 2021;11(1):237-45.

38. Schottel BL, Chifotides HT, Dunbar KR. Anion-π interactions. Royal Soc Chem. 2008;37:68-83.

39. Kharisma VD, Ansori ANM, Dian FA, Rizky WC, Dings TGA, Zainul R, et al. Molecular docking and dynamics simulation of entry inhibitor from Tamarindus indica bioactive compounds against SARS-CoV-2 infection via viroinformatics study. Biochem Cell Arch. 2021;21(2):3323-7.

40. Ansori ANM, Fadholly A, Proboningrat A, Antonius Y, Hayaza S, Susilo RJ. Novel Antiviral Investigation of Annona squamosa Leaf Extract against the Dengue Virus Type-2: In vitro Study. Pharmacogn J. 2021;13(2):456-62.

41. Kan X, Liu H, Pan Q, Li Z, Zhao Y. Anion-π interactions: From concept to application. Chin Chem Letters. 2018;29(2):262-6.

42. Kharisma VD, Ansori ANM, Nugraha AP. Computational study of Ginger (Zingiber officinale) as E6 inhibitor in human papillomavirus type 16 (HPV-16) infection. Biochem Cell Arch. 2020;20(1):3155-9.

43. Hartono, Suryawati B, Sari Y, Avicena A, Maryani, Sukmagautama C, et al. The effect of curcumin and virgin coconut oil towards cytokines levels in COVID-19 patients at Universitas Sebelas Maret Hospital, Surakarta, Indonesia. Pharmacogn J. 2022;14(1):216-25.

44. Risky WC, Jhivapranri MC, Kindi AA, Ansori ANM, Mustaq M. The pharmacological mechanism of quecetion as adjuvant therapy of COVID-19. Traditional Med Res. 2020;22:1-9.

45. Ansori ANM. Alpha-mangostin and gamma-mangostin isolated from mangosteen (Garcinia mangostana L.) as promising candidates against SARS-CoV-2: A bioinformatics approach. Indian J Forensic Med Toxicol. 2022;16(1):251-8.

46. Tacharina MR, Ansori ANM, Plumeniastuti H, Kusnito, Kunijasanti R, Hestianah EP. Beneficial effect of grinting grass (Cynodon dactylon) on the streptozotocin induced diabetes mellitus in the mice. Indian Vet J. 2020;97:35-8.

47. Naw SW, Probojati RT, Murtadio AAA, Ullah ME. Computational Drug Design Study of Curcuma longa L. Compound as HPV-16 Antiviral Candidate Against Cervical Cancer. SAINSTEK Int J Appl Sci Adv Technol Inform. 2022;11(1):1-6.

48. Ullah ME, Probojati RT, Murtadio AAA, Tamam MB, Naw WR. Revealing of Antiinflammatory Agent from Zingiber officinale var. Roscoe via IKK-B Inhibitor Mechanism through In Silico Simulation. SAINSTEK Int J Appl Sci Adv Technol Inform. 2022;11(1):14-9.

49. Ullah ME, Naw WR, Murtadio AAA, Tamam MB, Probojati RT. Molecular Mechanism of Black Tea (Camellia sinensis) as SARS-CoV-2 Spike Glycoprotein Inhibitor through Computational Approach. SAINSTEK Int J Appl Sci Adv Technol Inform. 2022;11(1):20-5.

50. Probojati RT, Murtadio AAA, Ullah ME, Naw WR, Turista DDR. Molecular Docking Study of HIV-1 Antiretroviral Candidate via Reverse Transcriptase Inhibitor from Zingiber officinale var. Roscoe. SAINSTEK Int J Appl Sci Adv Technol Inform. 2022;11(1):26-31.

51. Tamam MB, Naw WR, Ullah ME, Probojati RT, Murtadio AAA, Turista DDR. Virtual Screening of Kaempferia galanga L. Bioactive Compounds as HPV-16 Antiviral Mechanism Through E6 Inhibitor Activity. SAINSTEK Int J Appl Sci Adv Technol Inform. 2022;11(1):7-13.

---

**GRAPHICAL ABSTRACT**

**SARS-CoV-2**

*Portulaca oleracea* L.

*Illicium verum* Hook.
Aini NS, et al.: Bioactive Compounds from Purslane (Portulaca oleracea L.) and Star Anise (Illicium verum Hook) as SARS-CoV-2 Antiviral Agent via Dual Inhibitor Mechanism: In Silico Approach

**ABOUT AUTHORS**

Nur Sofiatul Aini is a student in general biology at State University of Surabaya, Indonesia. Her research focuses on ethnobotany, enzymology, food additive microbiology, and bioinformatics.

Rahadian Zainul has completed a Bachelor of Educational Chemistry in IKIP Padang, then continued his studies and obtained a Master of Chemistry at Universitas Andalas, and earned a Doctoral Chemistry degree at Universitas Andalas. He is a researcher on the design and modification of copper oxide for inactivation SARS-CoV-2 by stimulated indoor lights and a researcher on the design and modification of copper oxide by computation approach with DFTB+. He is also the Head of Cambiotics Research Center, Universitas Negeri Padang. The author has published 41 manuscripts in Scopus-indexed journals and also 8 h-index.

**Cite this article:** Aini NS, Kharisma VD, Widyananda MH, Murtadlo AAA, Probojati RT, Turista DDR, et al. Bioactive Compounds from Purslane (Portulaca oleracea L.) and Star Anise (Illicium verum Hook) as SARS-CoV-2 Antiviral Agent via Dual Inhibitor Mechanism: In Silico Approach. Pharmacogn J. 2022;14(4): 352-357.