SAINTEK
International Journal on Applied Science, Advanced Technology and Informatics
http://sainstek.ppj.unp.ac.id/index.php/sainstek

Computational Screening of Toxicity, Drug-like Molecule, and Bioactivity from Green Tea Phytochemical as Antiviral Candidate

Received 14 Desember 2022,
Accepted 21 Desember 2022,

DOI: 10.1039/sainstek/vol1-iss02/8

Priscilla Listiyani[1], Santika Lusia Utami[2], Dora Dayu Rahma Turista[3]*, Arbi Wiguna[4], Arini Wijayanti[5], Yuanita Rachmawati[6], Alyaa Farrah Dibha[7], Thobib Hasan[8], Muhammad Aldino Hafidzhah[9], Renadya Maulani Wijaya[9], Agus Mohammad Hikam[10], Ahmad Affan Ali Murtadlo[1], Muhammad Badrut Tamam[11], Sri Wahyuningsih[2], Nelson Chandra[9], Sin War Naw[12]

[1]Computational Virology Research Unit, Molecular Biology and Genetics Division, Generasi Biologi Indonesia Foundation, Gresik Indonesia.
[2]Faculty of Biology, Universitas Gadjah Mada, Yogyakarta, Indonesia.
[3]Educational Biology Department, Faculty of Teacher Training and Education, Mulawarman University, Samarinda, Indonesia.
[4]Zoology Division, Generasi Biologi Indonesia Foundation, Gresik, Indonesia.
[5]Department of Ecology and Evolutionary Biology, University of California Santa Cruz, Santa Cruz, United States.
[6]Department of Biology, Faculty of Science and Technology, UIN Sunan Ampel Surabaya, Surabaya, Indonesia.
[7]Chemistry Department, Faculty of Mathematics and Natural Sciences, Brawijaya University, Malang, Indonesia.
[8]Department of Biology, Faculty of Mathematics and Natural Sciences, IPB University, Bogor, Indonesia.
[9]Department of Bioinformatics, School of Life Sciences, Indonesia International Institute for Life-Sciences, East Jakarta, Indonesia.
[10]Faculty of Mathematics and Natural Sciences, Universitas Islam Malang, Malang, Indonesia.
[11]Department of Biology, Faculty of Sciences and Technology, Universitas Muhammadiyah Lamongan, Lamongan, Indonesia.
[12]Department of Chemistry, Myitkyina University, Myitkyina, Myanmar.

*Corresponding Author: doraturistaofficial@gmail.com

ABSTRACT

Viruses are obligate intracellular parasites because they can infect cells and hijack the gene expression process in host cells for the replication of viral genetic material. The mechanism of the viral life cycle is generally divided into three stages such as viral entry, genome replication, budding, and release. Several viruses can inhibit interferon signaling through the JAK/STAT pathway such as human cytomegalovirus (HCMV), HIV-1, murine hepatitis virus (MHV), severe acute respiratory syndrome coronavirus (SARS-CoV-2), & vaccinia virus (VACV). Antiviral drugs can be developed by

† Footnotes relating to the title and/or authors should appear here.
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/sainstek/vol1-iss02/8

studying how viruses evade the immune response, several drugs have been discovered but most of them are synthetic compounds that produce the use effect. Screening of drug candidate compounds can be carried out on a specific natural ingredient such as green tea used in this study. Scientific evidence of compounds from green tea as an antiviral agent is very little, this study is important because it is to screen the potential of compounds from green tea as an antiviral agent through computational approach. Green Tea phytochemical compounds are predicted to be antiviral based on *in silico* analysis. Antiviral candidate are EGCG, ECG, EGC, EC, & Catechin, they are drug-like molecules and have positive probabilities as antiviral agents.

Keywords: Antiviral, Computational Screening, Bioactivity, Green Tea, Phytochemical

INTRODUCTION

Viruses are obligate intracellular parasites because they can infect cells and hijack the gene expression process in host cells for the replication of viral genetic material[1,2]. The mechanism of the viral life cycle is generally divided into three stages such as viral entry, genome replication, budding, and release[3,4]. Virus replication begins with viral entry through an attachment mechanism with target receptors on the surface of the host cell, then the virus penetrates to the cytoplasm and carries out the genome replication stage[5,6]. When specific proteins and viral genomes have been formed, they will undergo assembly to form new virions and undergo maturation and then released out of the cell to infect other host cells[7,8]. The viral life cycle process also involves activities to evade the body's immune response, the virus can produce a protein to inhibit the recognition of immune cells or prevent host cells from releasing specific cytokines for natural antiviral activation responses such as interferon[9,10].

Viral infections are viral pathogen-associated molecular patterns (PAMPs) recognized by immune cells through host pattern recognition receptors (PRRs)[11,12]. PAMPs are present in viruses and not in host cells, thus enabling cells to carry out an immune response during infection[13]. Several types of PRRs to detect viral infections consist of RIG-I-like receptors (RLRs), Toll-like receptors (TLRs), and DNA sensors for the detection of proteins and nucleic acids from viruses[14,15]. These three proteins can be activated and then trigger transcription factors for the regulation of IFN expression. IFN can inhibit viral replication in host cells and trigger apoptotic signaling to reduce virus spread to other cells[16,17]. Several viruses can inhibit interferon signaling through the JAK/STAT pathway such as human cytomegalovirus (HCMV), HIV-1, murine hepatitis virus (MHV), severe acute respiratory syndrome coronavirus (SARS-CoV-2), & vaccinia virus (VACV)[18,19]. Antiviral drugs can be developed by studying how viruses evade the immune response, several drugs have been discovered but most of them are synthetic compounds that produce the use effect.

Screening of drug candidate compounds can be carried out on a specific natural ingredient such as green tea used in this study. Compounds in green tea consist of catechin, epigallocatechin-3-gallate (EGCG) CID, (−)-epicatechin-3-gallate (ECG) CID, (−)-epigallocatechin (EGC) and (−)-epicatechin (EC)[20]. Previous research has shown that green tea compounds have the potential to treat diseases such as diabetes, cancer, autoimmune disease, and others[21]. Scientific evidence of compounds from green tea as an antiviral agent is very little, this study is important because it is to screen the potential of compounds from green tea as an antiviral agent through an in silico approach.

METHOD

Compound retrieval

Green tea compounds such as catechin, (−)-epigallocatechin-3-gallate (EGCG), (−)-epicatechin-3-gallate (ECG), (−)-epigallocatechin (EGC) and (−)-epicatechin (EC) for ligand preparation was obtained from the PubChem database (https://pubchem.ncbi.nlm.nih.gov/). The information obtained from PubChem consists of Canonical SMILE and the 3D structure of the target compound. Visualization of the 3D structure of green tea compounds was carried out using PyMol v2.5 software with structural selection and atomic coloring techniques[22,23].

Druglikeness and toxicity prediction

Table 1. Green tea compound drug-like molecule

Compound	Pubchem CID	Predicted LD50 (mg/kg)	Predicted Toxicity Class	Average Similarity	Prediction Accuracy
EGCG	65064	1000	4	100%	100%
ECG	65056	1000	4	100%	100%
EGC	72277	1000	6	100%	100%
EC	72276	1000	6	100%	100%
Catechin	9064	1000	6	100%	100%

The ability of candidate compounds from green tea and the degree of similarity to drug molecules when triggering activity in the body were predicted on the Lipinski Rule of Five server (http://www.scfbio-iitd.res.in/software/drugdesign/lipinski.jsp).
Parameters for the determination of drug-like molecules on the server consists of molar refractivity, hydrogen acceptors & donors, molecular mass, and high lipophilicity[24]. Toxicity prediction on query compounds from green tea was carried out via the ProTox-II server (https://tox-new.charite.de/protox_II/). Prediction is done by referring to the LD50 value or the dose where 50% of the test subjects die after administration of the query compound[25,26].

Antiviral identification

Identification of compounds from green tea as an antiviral was done through the Wy2Drug PASSOnline server (http://www.pharmaexpert.ru/passonline/). Prediction works with Canonical SMILE data input and confidence score then the antiviral candidate compound with positive prediction results is obtained with activation probability (Pa)> inhibition probability (Pi)[27,28].

RESULT AND DISCUSSION

Revealing of drug-like molecule and toxicity

The parameters used in this study in determining drug-like molecules by referring to the Lipinski Rule of Five, this rule refers to the hydrogen bond donor (HBD), high lipophilicity (LogP), molecular weight (MM), hydrogen bond acceptor (HBA), & molar refractivity (MR), query compounds with drug-like molecule properties must follow at least two Lipinski rules[29,30]. Lipinski's rule consists of molar refractivity should be between 40-130, molecular mass less than 500 Dalton, less than 5 hydrogen bond donors & 10 for hydrogen bond acceptors[31,32]. Drug candidate compounds that follow the Lipinski Rule of Five are predicted to be able to pass through selectively permeable membranes, affect charge movement, and trigger passive transport[33,34]. Bioactive compounds from Green Tea consisting of EGCG, ECG, EGC, EC, & Catechin, were obtained from PubChem, then 3D visualization was performed using PyMol v2.5 software with color selection (Figure 1). All bioactive compounds in this study were predicted as drug-like molecules because all compounds follow more than two of Lipinski's rules (Table 1).

Table 2. The results of compound toxicity prediction

Compound	Pubchem CID	MM (g/mol)	LogP	HBD	HBA	MR
EGCG	65064	458.37	1.87	8	11	112.06
ECG	65056	442.37	1.44	7	10	110.04
EGC	72277	306.27	0.98	6	7	76.36
EC	72276	290.27	1.47	5	6	74.33
Catechin	9064	290.27	1.47	6	5	74.33

Toxicity tests were carried out on compounds from green tea via the ProTox-II server. Toxicity is determined by the LD50 or median lethal dose meaning the dose at which 50% of test subjects die upon exposure to a compound. LD50 values are classified into class I: fatal if swallowed (LD50 5), class II: fatal if swallowed (5 < LD50 50), class III: toxic if swallowed (50 < LD50 300), class IV: harmful if swallowed (300 < LD50 2000), class V: may be harmful if swallowed (2000 < LD50 5000) & class VI: non-toxic (LD50 > 5000)[35,36]. ProTox-II incorporates machine-

learning, propensities, molecular similarity, frequent features, based a total of 33 models for the prediction of various toxicity endpoints such as acute toxicity, carcinogenicity, hepatotoxicity, cytotoxicity, mutagenicity, immunotoxicity, & Tox21 pathways and toxicity targets[37]. The results of the prediction of the toxicity of the Green Tea compound showed that the LD50 value of all compounds was 1000 mg/kg with toxicity class IV – VI (Table 2). The toxicity of Green Tea compounds is classified as safe for use or consumption because in low doses.

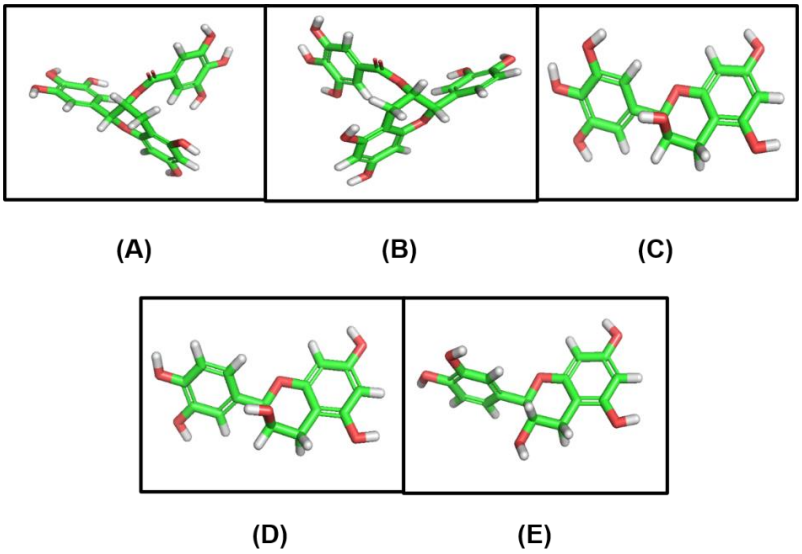

Figure 1. Molecular visualization of Green Tea compounds. (A) EGCG (B) ECG (C) EGC (D) EC & (E) Catechin.

The probability of antiviral candidate

Antiviral probability prediction on drug-like compounds from Green Tea is done through the PASSOnline server. This prediction aims to determine the antiviral probability by referring to the value of probability activation (Pa) and probability inhibition (Pi)[38]. Antiviral probabilities with medium confidence (Pa>0.3) were used in the study. Probability with medium confidence (Pa>0.3) was chosen to screen the potential of a bioactive compound with scientific evidence through a computational approach or based on data mining[39]. Predicted results of bioactivity as antiviral showed EGCG, ECG, EGC, EC, & Catechin is predicted as a candidate antiviral agent because it has Pa>0.3 (Table 3). Antiviral candidate compounds with Pa>0.3 should be re-selected through literature studies, it is for additional scientific evidence.

Table 3. The results of antiviral probability

Compound	Pubchem CID	Formula	SMILE Canonical	Antiviral Probability (Pa>0.3)	
				Pa	Pi
EGCG	65064	$C_{22}H_{18}O_{11}$	C1C(C(OC2=CC(=CC(=C21)O)O)C3=CC(=C(C(=C3)O)O)O)OC(=O)C4=CC(=C(C(=C4)O)O)O	0.771	0.003
ECG	65056	$C_{22}H_{18}O_{10}$	C1C(C(OC2=CC(=CC(=C21)O)O)C3=CC(=C(C=C3)O)O)OC(=O)C4=CC(=C(C(=C4)O)O)O	0.764	0.004
EGC	72277	$C_{15}H_{14}O_{7}$	C1C(C(OC2=CC(=CC(=C21)O)O)C3=CC(=C(C(=C3)O)O)O)O	0.712	0.005
EC	72276	$C_{15}H_{14}O_{6}$	C1C(C(OC2=CC(=CC(=C21)O)O)C3=CC(=C(C=C3)O)O)O	0.692	0.006
Catechin	9064	$C_{15}H_{14}O_{6}$	C1C(C(OC2=CC(=CC(=C21)O)O)C3=CC(=C(C=C3)O)O)O	0.692	0.006

Green tea catechins (GTCs) are reported to play an important role in the treatment of various diseases such as viruses. GTCs can be antiviral agents in cases of infection with HBV, HSV, EBV, Adenovirus, HIV, Influenza, DENV, JEV, TBEV, ZIKV, CHIKV, HTLV, Rotavirus, EBOV, PRRSV, & EV71[40]. The mechanism of GTCs triggers antiviral effects by inhibiting and decreasing the activity of the protein coding for the replication of the target virus. Based on the results of the literature study, compounds from Green Tea with Pa>0.3 which have potential as antiviral agents are EGCG, ECG, EGC, EC, & Catechin, these compounds can be recommended for further analysis.

CONCLUSION

Green Tea phytochemical compounds are predicted to be antiviral based on *in silico* analysis. Antiviral candidate are EGCG, ECG, EGC, EC, & Catechin, they are drug-like molecules and have positive probabilities as antiviral agents. We recommend these three compounds for further analysis such as molecular docking, dynamic simulation, target identification, and biological pathway simulations for additional scientific evidence.

REFERENCES

1. Xu J, Xu Z, Zheng W. A Review of the Antiviral Role of Green Tea Catechins. Molecules. 2017; 22(8): 1337. DOI: 10.3390/molecules22081337.
2. Mhatre S, Srivastava T, Naik S, Patravale V. Antiviral activity of green tea and black tea polyphenols in prophylaxis and treatment of COVID-19: A review. Phytomedicine. 2021; 85: 153286. DOI: 10.1016/j.phymed.2020.
3. Ansori ANM, Fadholly A, Proboningrat A, Antonius Y, Hayaza S, Susilo RJ, Inayatillah B, Sibero MT, Naw SW, Posa GAV, Sucipto TH, Soegijanto S. Novel Antiviral Investigation of Annona squamosa Leaf Extract against the Dengue Virus Type-2: In vitro Study. Phcog J. 2021; 13(2): 456-462. DOI: 10.5530/pj.2021.13.58
4. Ansori AN, Kharisma VD, Parikesit AA, Dian FA, Probojati RT, Rebezov M, Scherbakov P, Burkov P, Zhdanova G, Mikhalev A, Antonius Y, Pratama MRF, Sumantri NI, Sucipto TH, Zainul R. Bioactive Compounds from Mangosteen (Garcinia mangostana L.) as an Antiviral Agent via Dual Inhibitor Mechanism against SARS-CoV- 2: An In Silico Approach. Phcog J. 2022; 14(1): 85-90. DOI: 10.5530/pj.2022.14.12
5. Wijaya RM, Hafidzhah MA, Kharisma VD, Ansori ANM, Parikesit AP. COVID-19 In Silico Drug with Zingiber officinale Natural Product Compound Library Targeting the Mpro Protein. Makara J Sci. 2021; 25(3): 5. DOI: 10.7454/mss.v25i3.1244
6. 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: 839-857. DOI: 10.1007/978-3-030-63761-3_47.
7. Winarni D, Husna FN, Syadzha MF, Susilo RJK, Hayaza S, Ansori ANM, Alamsjah MA, Amin MNG, Wulandari PAC, Pudjiastuti P, Awang K. Topical Administration Effect of Sargassum duplicatum and Garcinia mangostana Extracts Combination on Open Wound Healing Process in Diabetic Mice. Scientifica. 2022; 2022: 9700794. DOI: 10.1155/2022/9700794.
8. Khairullah AR, Solikhah TI, Ansori ANM, Hanisia RH, Puspitarani GA, Fadholly A, Ramandinianto SC. Medicinal importance of Kaempferia galanga L. (Zingiberaceae): A comprehensive review. J Herbmed Pharmacol. 2021; 10: 281-288. DOI: 10.34172/jhp.2021.32
9. Kharisma VD, Probojati RT, Murtadlo AAA, Ansori ANM, Antonius Y, Tamam MB. Revealing Potency of Bioactive Compounds as Inhibitor of Dengue Virus (DENV) NS2B/NS3 Protease from Sweet Potato (Ipomoea batatas L.) Leaves. Indian J Forensic Med Toxicol. 2020; 15(1): 1627–1632. DOI: 10.37506/ijfmt.v15i1.13644
10. Kharisma VD, Agatha A, Ansori ANM, Widyananda MH, Rizky WC, Dings TGA, Derkho M, Lykasova I, Antonius Y, Rosadi I, Zainul R. Herbal combination from Moringa 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): 138-146.
11. Ansori ANM, Susilo RJK, Fadholly A, Hayaza S, Nugraha AP, Husen SA. Antidiabetes type 2 phytomedicine: Mangosteen (Garcinia Mangostana l.)-A review. Biochem Cell Arch. 2020; 20: 3173-3177. DOI: 10.35124/bca.2020.20.S1.3173
12. Khairullah AR, Solikhah TI, Ansori ANM, Fadholly A, Ramandinianto SC, Ansharieta R, Widodo A, Riwu KHP, Putri N, Proboningrat A, Kusala MKJ, Rendragraha BW, Putra ARS, Anshori A. A Review of an Important Medicinal Plant: Alpinia galanga (L.)

Willd. Sys Rev Pharm. 2020; 11(10): 387-395. DOI: 10.31838/srp.2020.10.62

13. Kharisma VD, Widyananda MH, Ansori ANM, Nege AS, Naw 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. 9(4): 435-445.
14. Kharisma VD, Ansori ANM, Widyananda MH, Utami SL, Nugraha AP. Molecular simulation: The potency of conserved region on E6 HPV-16 as a binding target of black tea compounds against cervical cancer. Biochem Cell Arch. 2020; 20: 2795-2802. DOI: 10.35124/bca.2020.20.S1.2795
15. Widyananda MH, Pratama SK, Samoedra RS, Sari FN, Kharisma VD, Ansori ANM, Antonius Y (2021) 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 9(4): 484–496.
16. Tacharina MR, Ansori ANM, Plumeriastuti H, Kusnoto , Kurnijasanti R, Hestianah EP. Beneficial effect of grinting grass (Cynodon dactylon) on the streptozotocin induced diabetes mellitus in the mice. Indian Vet J. 2020; 97(4): 35-38.
17. Wahyuni DK, Ansori ANM, Vidiyanti F. GC-MS analysis of phytocomponents in methanolic extracts of leaf-derived callus of Justicia gendarussa Burm.f. Biosci Res. 2017;14(3):668-677.
18. Husen SA, Winarni D, Salamun, Ansori ANM, Susilo RJK, Hayaza S. Hepatoprotective Effect of Gamma-mangostin for Amelioration of Impaired Liver Structure and Function in Streptozotocin-induced Diabetic Mice. IOP Conf Ser: Earth Env Sci. 2019; 217(1): 012031. DOI: 10.1088/1755-1315/217/1/012031
19. Ansori ANM, Kusala MKJ, Irawan H, Putri N, Fadholly A, Proboningrat A, Rukmana Siti, Karni I, Anisa AK, Adrianto H. Citrus reticulata extract as biocides to control Aedes aegypti, the vector of dengue. Biosci Res. 2018; 15(3): 1661-1665.
20. Ansori ANM, Sucipto TH, Chylichcova S, Padmi H, Kharisma VD, Widyananda MH, Ullah E, Gumenyuk O, Prasedya ES, Sibero MT, Bratishko N, Zainul R. Macroalgae Bioactive Compounds for the Potential Antiviral of SARS-CoV-2: An In Silico Study. Journal of Pure and Applied Microbiology. 2022; 16(2): 1018-1027. DOI: 10.22207/JPAM.16.2.26
21. Fadholly A, Ansori ANM, Utomo B. Anticancer Effect of Naringin on Human Colon Cancer (WiDr Cells): In Vitro Study. Research Journal of Pharmacy and Technology. 2022; 15(2): 885-888. DOI: 10.52711/0974-360X.2022.00148
22. Dibha AF, Wahyuningsih S, Ansori ANM, Kharisma VD, Widyananda MH, Parikesit AA, Sibero MT, Probojati RT, Murtadlo AAA, Trinugroho JP, Sucipto TH, Turista DDR, Rosadi I, Ullah ME, Jakhmola V, Zainul R. Utilization of Secondary Metabolites in Algae Kappaphycus alvarezii as a Breast Cancer Drug with a Computational Method. Pharmacognosy Journal. 2022; 14(3): 536-543. DOI: 10.5530/pj.2022.14.68
23. Aini NS, Ansori ANM, Kharisma VD, Syadzha MF, Widyananda MH, Murtadlo AA, et al. Potential Roles of Purslane (Portulaca oleracea L.) as Antimetabolic Syndrome: A Review. Pharmacognosy Journal. 2022; 14(3): 710-714. DOI: 10.5530/pj.2022.14.90
24. Listiyani P, Kharisma VD, Ansori AN, Widyananda MH, Probojati RT, Murtadlo AA, et al. In Silico Phytochemical Compounds Screening of Allium sativum Targeting the Mpro of SARS-CoV-2. Pharmacognosy Journal. 2022; 14(3): 604-609. DOI: 10.5530/pj.2022.14.78
25. Ansori ANM, Fadholly A, Hayaza S, Susilo RJK, Inayatillah B, Winarni D, Husen SA. A Review on Medicinal Properties of Mangosteen (Garcinia mangostana L.). Res J Pharm Techol. 2020; 13(2):974-982. doi: 10.5958/0974-360X.2020.00182.1
26. Husen SA, Wahyuningsih SPA, Ansori ANM, Hayaza S, Susilo RJK, Winarni D, Punnapayak H, Darmanto W. Antioxidant Potency of Okra (Abelmoschus esculentus Moench) Pods Extract on SOD Level and Tissue Glucose Tolerance in Diabetic Mice. Res J Pharm Technol. 12(12): 5683. doi: 10.5958/0974-360X.2019.00983.1
27. Husen SA, Setyawan MF, Syadzha MF, Susilo RJK, Hayaza S, Ansori ANM, Alamsjah MA, Ilmi ZN, Wulandari PAC, Pudjiastuti P, Awang P, Winarni D. A Novel Therapeutic effects of Sargassum ilicifolium Alginate and Okra (Abelmoschus esculentus) Pods extracts on Open wound healing process in Diabetic Mice. Research J. Pharm. and Tech 2020; 13(6): 2764-2770. doi: 10.5958/0974-360X.2020.00491.6
28. Kharisma VD, Kharisma SD, Ansori ANM, Kurniawan HP, Witaningrum AM, Fadholly A, Tacharina MR. Antiretroviral Effect Simulation from Black Tea (Camellia sinensis) via Dual Inhibitors Mechanism in HIV-1 and its Social Perspective in Indonesia. Res J Pharm Technol. 2021; 14(1): 455-460. doi: 10.5958/0974-360X.2021.00083.4

29. Fadholly A, Ansori ANM, Kharisma VD, Rahmahani J, Tacharina MR. Immunobioinformatics of Rabies Virus in Various Countries of Asia: Glycoprotein Gene. Res J Pharm Technol. 2021; 14(2): 883-886. doi: 10.5958/0974-360X.2021.00157.8
30. Ansori ANM, Fadholly A, Proboningrat A, Hayaza S, Susilo RJK, Naw SW, Posa GAV, Yusrizal YF, Sibero MT, Sucipto TH, Soegijanto S. In vitro antiviral activity of Pinus merkusii (Pinaceae) stem bark and cone against dengue virus type-2 (DENV-2). Res J Pharm Technol. 2021; 14(7):3705-8. doi: 10.52711/0974-360X.2021.00641
31. 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. Research Journal of Pharmacy and Technology 2021; 14(10):5551-7. doi: 10.52711/0974-360X.2021.00967
32. Husen SA, Ansori ANM, Hayaza S, Susilo RJK, Zuraidah AA, Winarni D, Punnapayak H, Darmanto W. Therapeutic Effect of Okra (Abelmoschus esculentus Moench) Pods Extract on Streptozotocin-Induced Type-2 Diabetic Mice. Res J Pharm Technol. 2019; 12(8):3703-3708. doi: 10.5958/0974-360X.2019.00633.4
33. Ansori ANM, Kharisma VD, Solikhah TI. Medicinal properties of Muntingia calabura L.: A Review. Res J Pharm Technol. 2021; 14(8):4509-2. doi: 10.52711/0974-360X.2021.00784
34. Proboningrat A, Kharisma VD, Ansori ANM, Rahmawati R, Fadholly A, Posa GAV, Sudjarwo SA, Rantam FA, Achmad AB. In silico Study of Natural inhibitors for Human papillomavirus-18 E6 protein. Res J Pharm Technol. 2022; 15(3):1251-6. doi: 10.52711/0974-360X.2022.00209
35. Kharisma VD, Ansori ANM, Jakhmola V, Rizky WC, Widyananda MH, Probojati RT, Murtadlo AAA, Rebezov M, Scherbakov P, Burkov P, Matrosova Y, Romanov A, Sihombing MAEM, Antonius Y, Zainul R. Multi-strain human papillomavirus (HPV) vaccine innovation via computational study: A mini review. Res J Pharm Technol. 2022; 15(8).
36. Naw SW, Probojati RT, Murtadlo, AAA, Ullah, ME. (2022). Computational Drug Design Study of Curcuma longa L. Compound as HPV-16 Antiviral Candidate Against Cervical Cancer. SAINSTEK International Journal on Applied Science, Advanced Technology and Informatics, 1(01), 1–6.
37. Ullah ME, Probojati RT, Murtadlo AAA, Tamam MB, Naw WR. Revealing of Antiinflamatory Agent from Zingiber officinale var. Roscoe via IKK-B Inhibitor Mechanism through In Silico Simulation. SAINSTEK International Journal on Applied Science, Advanced Technology and Informatics. 2022; 1(01): 14–19.
38. Ullah ME, Naw WR, Murtadlo AAA, Tamam MB, Probojati RT. Molecular Mechanism of Black Tea (Camellia sinensis) as SARS-CoV-2 Spike Glycoprotein Inhibitor through Computational Approach. SAINSTEK International Journal on Applied Science, Advanced Technology and Informatics. 2022; 1(01): 20–25.
39. Probojati RT, Murtadlo 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 International Journal on Applied Science, Advanced Technology and Informatics. 2022; 1(01): 26–31.
40. Tamam MB, Naw WR, Ullah ME, Probojati RT, Murtadlo AAA, Turista DDR. Virtual Screening of Kaempferia galanga L. Bioactive Compounds as HPV-16 Antiviral Mechanism Through E6 Inhibitor Activity. SAINSTEK International Journal on Applied Science, Advanced Technology and Informatics. 2022; 1(01): 7–13.