Biomedical & Pharmacology Journal, March 2025. Vol. **18**(1), p. 929-938

Inhibitory Action of Selected Alkaloids Targeting the Non-Structural Protein-1 (NS1) of Dengue Virus Type-4 (DENV4) *in silico*

Jerylle Joie Bautista, Cherry Mae Delos Santos, Jherby Kyle Teodoro and Dyanne Jane Cid Duldulao*

Natural and Applied Sciences Department, Nueva Ecija University of Science and Technology, Cabanatuan City, Philippines.
*Corresponding Author E-mail:dyannejaned@gmail.com

https://dx.doi.org/10.13005/bpj/3141

(Received: 31 December 2024; accepted: 07 March 2025)

Dengue fever has become a significant public health concern in recent years due to its high morbidity and notable mortality rates. This study intends to explore the potential inhibitory effects of phytochemicals derived from well-known toxic and medicinal alkaloid metabolites against the Non-structural Protein-1 (NS1) of the Dengue virus serotype 4 (DENV4). The DENV4-NS1 protein plays a crucial role in the replication and maturation of the virus within host cells. For this investigation, 20 alkaloids and 3 commercially available drug candidates targeting the Dengue virus were selected. The three-dimensional structure of DENV4-NS1 was chosen based on a literature review and identified in related research. The drug-likeness of the selected compounds was assessed through Absorption, Distribution, Metabolism, and Excretion (ADME) analysis, and their compliance with Lipinski's Rule of Five (RO5) was evaluated using the SwissADME web tool. The drug-likeness prediction results indicated that 19 out of the 20 alkaloids exhibited promising pharmacological properties. These alkaloids were then docked with DENV4-NS1 using AutoDock Vina, and 8 of them displayed stronger and more stable binding interactions than the model drugs (binding affinity = -8.1 kcal/mol), suggesting their potential as DENV4-NS1 inhibitors. This study also highlights the novel inhibitory activity of Lobeline against the dengue virus. In conclusion, the 19 phytochemicals identified in this study demonstrate significant inhibition potential against Dengue Virus 4 and warrant further exploration in drug development research.

Keywords: Alkaloids; antiviral; AutoDock Vina; dengue virus; in silico; molecular docking.

Dengue is a viral disease spread by mosquitoes, with symptoms resembling those of the flu. In some cases, the infection can develop into more serious conditions, such as dengue hemorrhagic fever or dengue shock syndrome, both of which can be fatal. Dengue virus (DENV) is recognized as a severe public health threat enlisting a large number of infections and deaths commonly in tropical and subtropical regions.[1] In the Philippines, the Department of Health (DOH) reports thousands of DENV infections yearly where an estimate of DENV infections increased from 46,300 to 131,000 cases in a span of five years.[2] DENV, classified within the flaviviral class and the flavivirus genus, has four distinct serotypes designated Dengue Virus 1 to 4 (DENV-1 to DENV-4). Among these serotypes, DENV-4 exhibits a robust correlation with severe conditions like the Dengue Shock Syndrome (DSS) and Dengue Hemorrhagic Fever (DHF).[3] Studies show

the prevalence of DENV-4 in a fatal case in Brazil, [4] and DENV-4 as the cause of dengue outbreak in Indonesia.[5]

Several treatment approaches have been explored against dengue virus and while there remains no targeted treatment for dengue, the most effective approach lies in the prevention of dengue infection.[6] Traditional approaches to the use of natural products combined with advances in bioinformatics have also been explored. Research has shown that alkaloids possess strong antiviral properties against both dengue and Zika viruses. Specifically, these compounds inhibit viral infection during the later phases of the replication process.[7]

This computational study aimed to explore the potential of 20 toxic alkaloids as inhibitors of the DENV- 4 NS1. Specifically, this focused on screening the identified alkaloids using ADME analysis; determining the binding affinity of the ligands and the NS1 protein of DENV-4; and visualizing the interaction between the ligands and the protein.

MATERIALS AND METHODS

Preparation of the Target Protein and its Binding Site Prediction

In molecular docking experiments, the structural integrity of the target protein is important and thus preparation and optimization of the structure is performed. Structure of the target DENV-NS1 was adopted from the study of Qaddir et al. Binding sites of the selected protein were

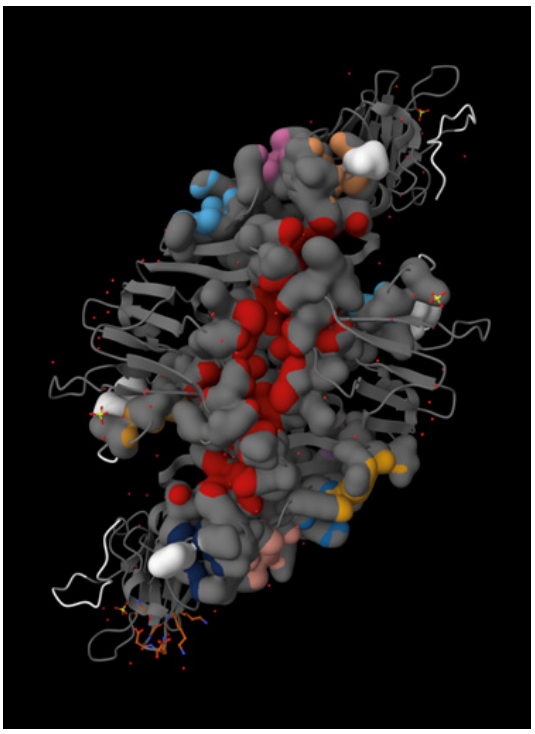


Fig. 1. Predicted binding pockets for DENV4-NS1 with pocket 1 shown in red

Table 1. Protein binding pockets predicted by PrankWeb server

Pocket No.	Score	Probability	Centers (x,y,z)	No. of residues in the binding site
1	45.51	0.971	x = 108.7238, y = -9.3166, z = 36.2464	60
2	2.52	0.071	x = 118.9673, y = -3.2772, z = 27.1814	11
3	2.50	0.070	x = 125.2846, y = -31.178, z = 33.2261	6
4	2.25	0.055	x = 98.3104, y = 15.6642, z = 27.0153	10
5	2.24	0.055	x = 98.4323, y = -15.7968, z = 27.4074	9
6	2.18	0.051	x = 119.6676, y = -34.7795, z = 27.6153	10
7	1.99	0.041	x = 108.2573, y = 22.7163, z = 29.3349	6
8	1.84	0.034	x = 91.6883, y =-19.7294, z = 34.8801	10
9	1.82	0.034	x = 112.4306, y = -27.7232, z = 17.8029	8
10	1.59	0.024	x = 108.9997, y = -41.2763, z = 28.9215	6
11	1.50	0.021	x = 111.4426, y = -30.9982, z = 13.8495	6
12	1.50	0.021	x = 106.5077, y = 11.5905, z = 13.4737	6
13	1.41	0.018	x = 119.2721, y = 18.9758, z = 36.4172	8
14	1.37	0.017	x = 126.438, y = 0.8139, z = 35.1035	9
15	1.31	0.015	x = 98.3137, y = -38.8671, z = 36.4872	9

predicted using the web server PrankWeb (https://prankweb.cz/).

Drug-likeness Prediction of the Ligands

The ligands in this study include the selected twenty alkaloids that were gathered from literature, [8,9,10] and three model drugs (doxycycline, acetaminophen, and balapiravir) that are commonly used by patients infected by the dengue virus. Drug-likeness prediction facilitates the screening of the ligands based on their Absorption, Distribution, Metabolism, Excretion (ADME) of the ligands. Canonical SMILES of the compounds collected from PubChem (https://pubchem.ncbi.nlm.nih.gov) were acquired as input for simulation in SwissADME web tool (http://www.swissadme.ch) to assess the ADME. This method filters the selection of ligands based on the drug-likeness of the metabolites. The rule of five delineated the relationship between pharmacokinetic and physicochemical parameters, [11] wherein ideal compounds should have a molecular weight of less than 500 Da, the number of hydrogen bond donors and hydrogen bond acceptors should be less than 5 and 10, respectively, and the octanol-water partition coefficient should be less than 5. [12]

Optimization of Ligand Structure

The ligands with suitable drug-like character were imported to UCSF Chimera software using the PubChem CID or structures files stored in .sdf file format to facilitate ligand optimization. The minimized ligands were saved in .pdb format, while the dock-prepared ligands were stored in .mol2 format, both of which were then prepared for molecular docking.

Molecular Docking (MD) Simulation

Molecular dynamics (MD) analysis was

Table 2. Ligands subjected to drug-likeness prediction

Ligands	PubChem ID	Canonical Smiles
Model drugs		
Acetaminophen	1983	CC(=O)NC1=CC=C(C=C1)O
Balapiravir	11691726	CC(C)C(=O)OCC1(C(C(C(O1)N2C=CC(=NC2=O)N)OC(=O)C(C)C)OC(=O)C(C)C)N=[N+]=[N-]
Doxycycline	54671203	CC1C2C(C3C(C(=O)C(=C(C3(C(=O)C2=C(C4=C1C=CC=C4O)O)O)O)C(=O)N)N(C)C)O
Alkaloids		
(+)-erythravine	11231853	COC1=C(C=C2C(=C1)CCN3C24CC(C=CC4=CC3)O)OC
(+)-xylopine	431059	COC1=CC2=C(C=C1)C3=C4C(C2)NCCC4=CC5=C3OCO5
Arecoline	2230	CN1CCC=C(C1)C(=O)OC
Berberine	2353	COC1=C(C2=C[N+]3=C(C=C2C=C1)C4=CC5=C(C=C4CC3)OCO5)OC
Caffeine	2519	CN1C=NC2=C1C(=O)N(C(=O)N2C)C
Cocaine	446220	CN1C2CCC1C(C(C2)OC(=O)C3=CC=CC=C3)C(=O)OC
Galantamine	9651	CN1CCC23C=CC(CC2OC4=C(C=CC(=C34)C1)OC)O
Geissospermine	5281401	CCC1CN2CCC34C2CC1C5C3N(C(OC5)C(C6CC7C8=C(CCN7CC6=CC)C9=CC=CC=C9N8)C(=O)OC)C1=CC=CC=C41
Harmine	5280953	CC1=NC=CC2=C1NC3=C2C=CC(=C3)OC
Huperzine A	449069	CC=C1C2CC3=C(C1(CC(=C2)C)N)C=CC(=O)N3
Isorynchophylline	3037048	CCC1CN2CCC3(C2CC1C(=COC)C(=O)OC)C4=CC=CC=C4NC3=O
Lobeline	5288703	CN1C(CCCC1CC(=O)C2=CC=CC=C2)CC(C3=CC=CC=C3)O
Montanine	11087935	COC1C=C2C(CC1O)N3CC2C4=CC5=C(C=C4C3)OCO5
Morphine	5288826	CN1CCC23C4C1CC5=C2C(=C(C=C5)O)OC3C(C=C4)O
Nantenine	197001	CN1CCC2=CC(=C(C3=C2C1CC4=CC5=C(C=C43)OCO5)OC)OC
Nicotine	89594	CN1CCCC1C2=CN=CC=C2
Physostigmine	5983	CC12CCN(C1N(C3=C2C=C(C=C3)OC(=O)NC)C)C
Piperine	638024	C1CCN(CC1)C(=O)C=CC=CC2=CC3=C(C=C2)OCO3
Salsoline	46695	CC1C2=CC(=C(C=C2CCN1)O)OC
Vinpocetine	443955	CCC12CCCN3C1C4=C(CC3)C5=CC=CC=C5N4C(=C2)C(=O)OCC

conducted using the free software AutoDock Vina, following the method described in a previous study.[13] The protein's binding site was identified, and the grid size was extended (27.8597Å × 54.7942Å × 23.0007Å) to include all potential interaction sites. The screened ligands were retrieved and docked into the target protein's binding pocket. The MD simulations were carried out using flexible docking, allowing both the protein and ligands to rotate freely, ensuring flexibility for the receptor and the ligands. The results were analyzed based on the binding affinity, with more negative values indicating stronger ligand-protein binding.[14]

Interaction Visualization

Root mean square deviation (RMSD) analysis was conducted using the BIOVIA Discovery Studio Visualizer. The interacting sites and the intermolecular forces involved, such as conventional hydrogen bonds, carbon-hydrogen bonds, alkyl interactions, and van der Waals forces, were examined and visualized for further analysis.

RESULTS

Protein Binding Site Prediction

Functionality of a protein relies on its structure and the interactions it forms with other molecules. Binding pockets of the target protein, NS1 of DENV 4 was predicted by PrankWeb server (Table 1).

Drug-likeness Prediction of the Ligands

A total of twenty-three ligands were used in this study consisting of twenty alkaloids and

Table 3. Drug-likeness prediction of the ligands

Ligands	Lipinski's Rule of Five					
	Molecular weight (MW < 500 Da)	No. of H Bond Acceptors (HBAs <5)	No.of H Bond Donor (HBDs <10)	LogP (LogP<5)	No. of Violation	Drug-likeness (If ≤ 1, yes; >1, no)
Model drugs						
Doxycycline	444.43	9	6	1.61	1	Yes
Balapiravir	494.50	12	1	3.22	1	Yes
Acetaminophen	151.16	2	2	1.21	0	Yes
Alkaloids						
(+)-erythravine	299.36	4	1	2.81	0	Yes
(+)-xylopine	295.33	4	1	3.12	0	Yes
Arecoline	155.19	3	0	2.26	0	Yes
Berberine	336.36	4	0	0.00	0	Yes
Caffeine	194.19	3	0	1.79	0	Yes
Cocaine	303.35	5	0	3.21	0	Yes
Galantamine	287.35	4	1	2.64	0	Yes
Geissospermine	632.83	5	1	5.01	2	No
Harmine	212.25	2	1	2.07	0	Yes
Huperzine A	242.32	2	2	2.41	0	Yes
Isorynchophylline	384.47	5	1	3.68	0	Yes
Lobeline	337.46	3	1	3.32	0	Yes
Montanine	301.34	5	1	2.85	0	Yes
Morphine	285.34	4	2	2.69	0	Yes
Nantenine	339.39	5	0	3.54	0	Yes
Nicotine	162.23	2	0	2.14	0	Yes
Physostigmine	275.35	3	1	2.83	0	Yes
Piperine	285.34	3	0	3.38	0	Yes
Salsoline	193.24	3	2	2.26	0	Yes
Vinpocetine	350.45	3	0	3.28	0	Yes

Table 4. Binding affinity values of the ligands

Ligands	Binding Affinity (kcal/mol)
Model drugs	
Balapiravir	-8.1
Doxycycline	-6.6
Acetaminophen	-5.9
Alkaloids	
Lobeline	-9.0
(+)-xylopine	-8.9
Berberine	-8.8
Morphine	-8.67
Piperine	-8.5
Galantamine	-8.3
Cocaine	-8.23
(+)-erythravine	-8.1
Montanine	-7.9
Vinpocetine	-7.89
Huperzine A	-7.89
Physostigmine	-7.77
Harmine	-7.3
Nantenine	-7.23
Isosrynchophylline	-6.87
Salsoline	-6.45
Caffeine	-6.2
Nicotine	-5.6
Arecoline	-5.33

three model drugs (Table 2). These ligands were subjected to ADME analysis using the Lipinski rule of 5 to evaluate their drug-likeness (Table 3).

Molecular Docking Simulation

Nineteen ligands (Table 4) with predicted drug-likeness were screened using the AutoDock Vina software to further select the ligand with potential antiviral activity against the DEV4-NS1. Most stable interactions were also visualized for selected ligands (Figure 2).

DISCUSSION

Protein Binding Site Prediction

Identification of binding sites dictates the possible binding ability of a protein with a ligand. This relates to the druggability of a protein, a property that determines the successful interaction of the protein to drug-like ligands that is necessary for rational drug design. [15] Utilized for this binding site determination is PrankWeb, an open-source web server that provides reliable predictions of protein binding sites by exploring ligand-binding areas on the protein. [16] The analysis identified a total of fifteen pockets, ranked from the highest to lowest based on predicted ligandability and probability scores, with pocket 1 having the highest values and pocket 15 the lowest (Table 1). Pocket 1 showed the highest pocket and probability scores of 45.51 and 0.971, respectively, and a total of 60 amino acid residues in the predicted binding pocket (Figure 1). These predicted binding residues and centers for pocket 1 were chosen as the target sites for the subsequent docking analysis.

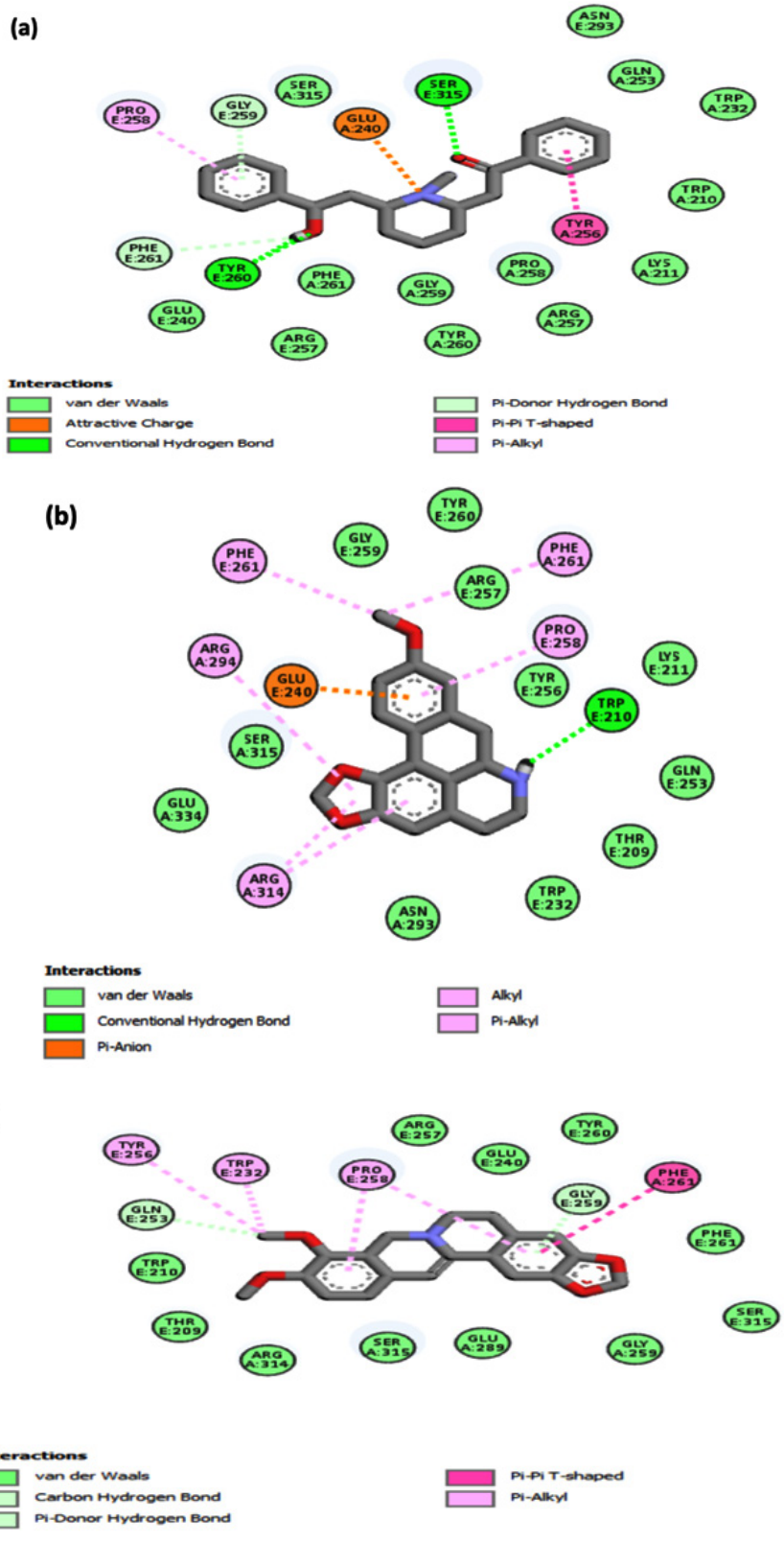
Drug-likeness Prediction of the Ligands

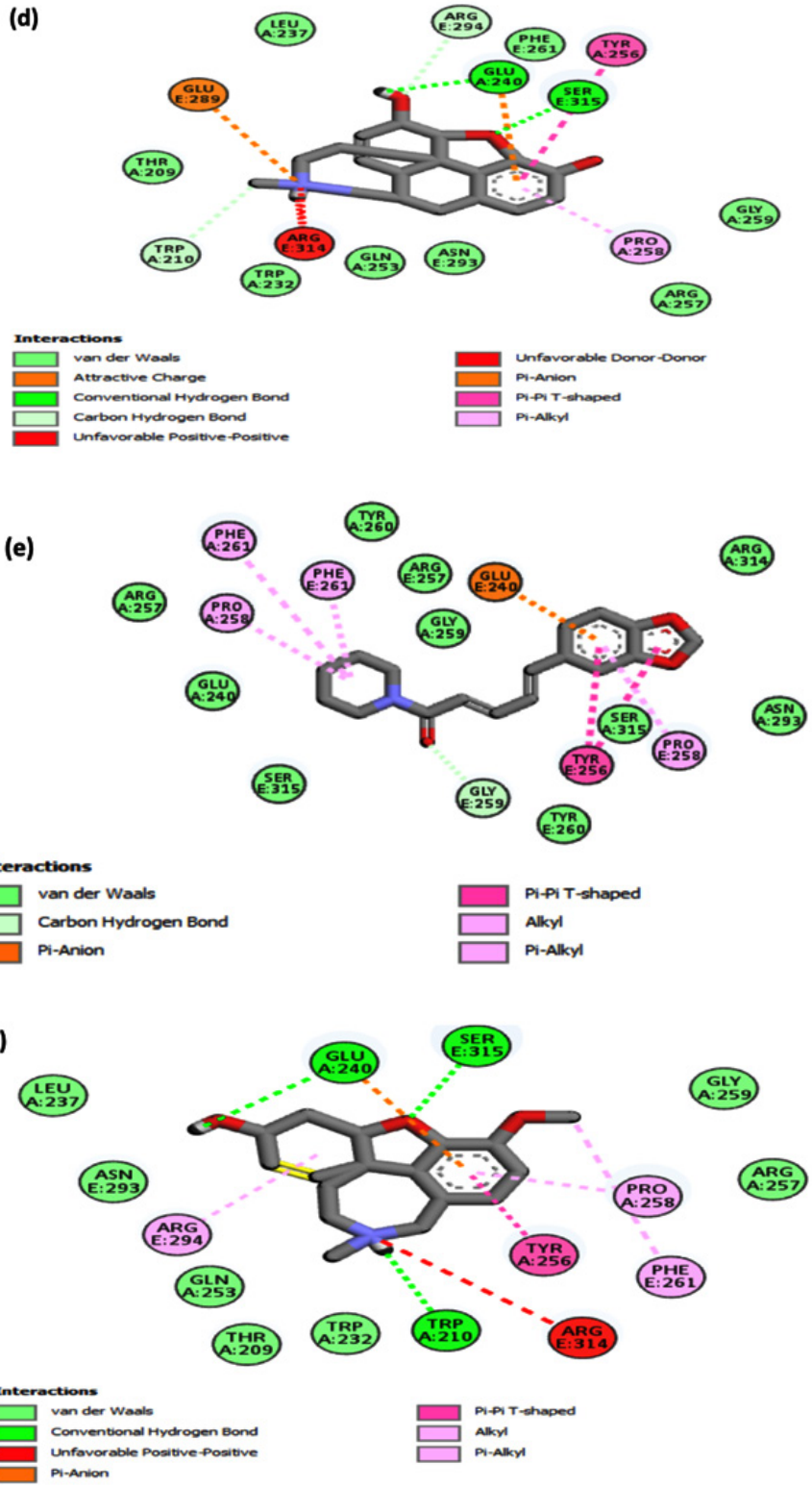
Lipinski screening sets the criteria for a potential drug-like molecule to have good absorption or drug permeability based on the number of H bonds acceptor (<5) and donor (<10), the molecular weight (<500 Da) and lipophilicity (Log P value <5).[17] A violation of at least two of the criteria would render the molecule a poor candidate due to low permeability, oral solubility, and poor bioavailability. [18] Those ligands with less than 2 violations were selected for further analysis. Nineteen of the twenty alkaloids passed all the pharmacokinetic standards without any violations indicating good biocompatibility. The alkaloid Geissospermine had 2 violations and was filtered out for the succeeding simulations while all the model drugs met the given criteria (Table 3).

Molecular Docking Simulation

Molecular docking is a computational technique that simulates protein and ligand interactions under physiological conditions and determines the stability of a given protein-ligand complex. [19] The docking simulation explores all possible orientations within the protein binding site. The stability of the interaction is quantified by the energy associated with each pose given that a stable complex equals a more negative binding affinity value. [20]

Three model drugs and nineteen alkaloids were docked into the determined pocket of the protein and binding affinities were reported in Table 4. Balapiravir (-8.1 kcal/mol) has the notable highest negative binding affinity compared to the other model drugs, Doxycycline (-6.6 kcal/mol) and Acetaminophen (-5.9 kcal/mol). This shows that among the model drugs used for management


(a)
ASN E:293
GLN A:253
TRP A:232
SER A:315
SER E:315
PRO E:258
GLY E:259
GLU A:240
TRP A:210
TYR A:256
PHE E:261
TYR E:260
PHE A:261
GLY A:259
PRO A:258
LYS A:211
GLU E:240
ARG A:257
ARG E:257
TYR A:260
Interactions
van der Waals
Attractive Charge
Conventional Hydrogen Bond
Pi-Donor Hydrogen Bond
Pi-Pi T-shaped
Pi-Alkyl
(b)
TYR E:260
GLY E:259
PHE E:261
PHE A:261
ARG E:257
PRO E:258
ARG A:294
LYS E:211
GLU E:240
TYR E:256
TRP E:210
SER A:315
GLN E:253
GLU A:334
THR E:209
ARG A:314
TRP E:232
ASN A:293
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Anion
Alkyl
Pi-Alkyl
(c)
ARG E:257
TYR E:260
TYR E:256
GLU E:240
TRP E:232
PRO E:258
PHE A:261
GLY E:259
GLN E:253
PHE E:261
TRP E:210
SER E:315
THR E:209
SER A:315
GLU A:289
GLY A:259
ARG A:314
Interactions
van der Waals
Carbon Hydrogen Bond
Pi-Donor Hydrogen Bond
Pi-Pi T-shaped
Pi-Alkyl


(d)
LEU A:237
ARG E:294
PHE E:261
TYR A:256
GLU A:240
SER E:315
GLU E:289
THR A:209
GLY A:259
ARG E:314
TRP A:210
GLN A:253
ASN E:293
PRO A:258
TRP A:232
ARG A:257
Interactions
van der Waals
Attractive Charge
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Unfavorable Positive-Positive
Unfavorable Donor-Donor
Pi-Anion
Pi-Pi T-shaped
Pi-Alkyl
(e)
TYR A:260
PHE A:261
ARG A:314
PHE E:261
ARG E:257
GLU E:240
ARG A:257
PRO A:258
GLY A:259
GLU A:240
ASN A:293
SER A:315
PRO E:258
TYR E:256
SER E:315
GLY E:259
TYR E:260
Interactions
van der Waals
Carbon Hydrogen Bond
Pi-Anion
Pi-Pi T-shaped
Alkyl
Pi-Alkyl
(f)
SER E:315
GLU A:240
LEU A:237
GLY A:259
ASN E:293
ARG A:257
PRO A:258
ARG E:294
TYR A:256
PHE E:261
GLN A:253
THR A:209
TRP A:232
TRP A:210
ARG E:314
Interactions
van der Waals
Conventional Hydrogen Bond
Unfavorable Positive-Positive
Pi-Anion
Pi-Pi T-shaped
Alkyl
Pi-Alkyl

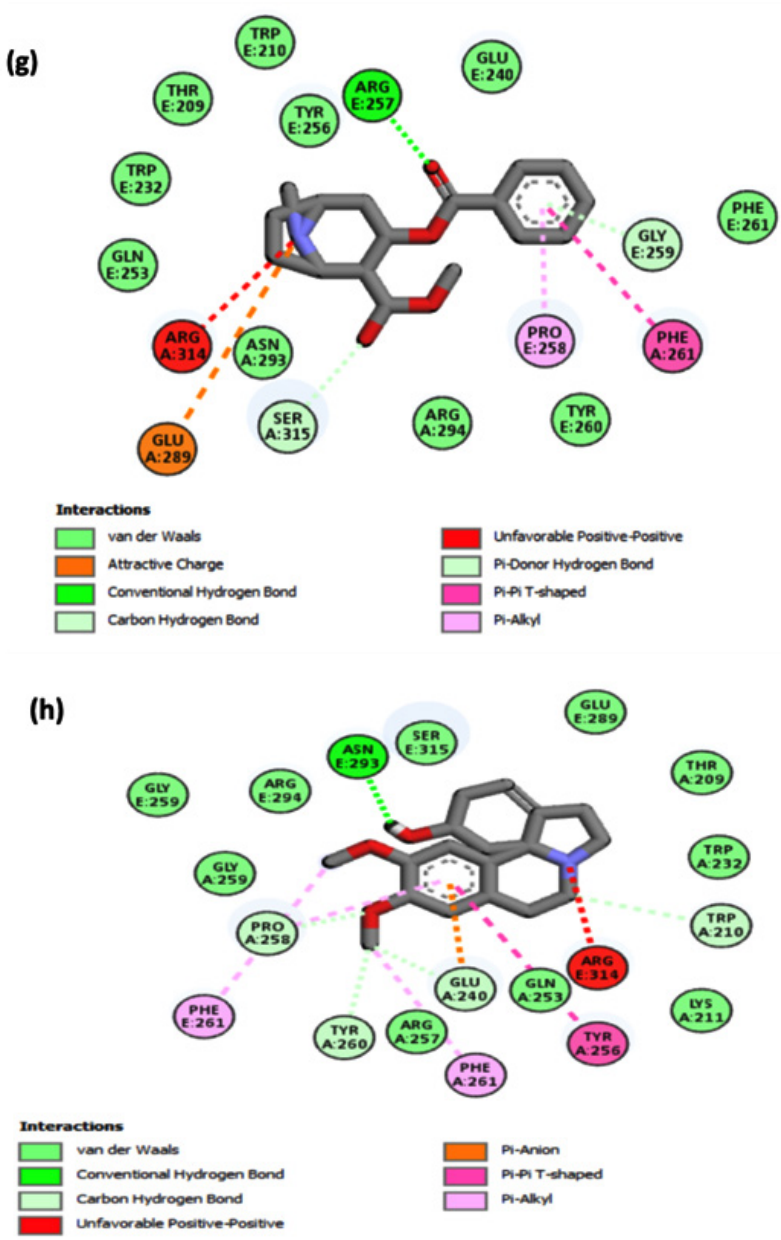


Fig. 2. Binding interactions between (a) Lobeline, (b) (+)-xylopine, (c) Berberine (d) Morphine, (e) Piperine, (f) Galantamine, (g) Cocaine, (h) (+)-erythravine and the DENV4-NS1 binding pocket

of dengue virus symptoms, Balapiravir has the most stable interaction with the binding site of DENV4- NS1. Binding affinity scores of the alkaloids were analyzed and compared to the value for Balapiravir. Seven compounds, Lobeline, (+)-xylopine, Berberine, Morphine, Piperine, Galantamine, Cocaine, have higher affinity values than the model drugs relating to more stable interactions. The alkaloid (+)-erythravine showed equal binding affinity with Balapiravir. These 8 alkaloids with the most stable interactions were subjected to interaction analysis to elucidate the types of interactions established between the ligand and the specific amino acids within the protein binding pocket (Figure 2).

CONCLUSION

In this study, ADME drug-likeness prediction, molecular docking simulations, and interaction visualization screened out 8 alkaloids with good pharmacological characteristics and stable interactions with the binding pocket of DENV4-NS1. Among the 8 selected alkaloids, Lobeline was calculated to have the highest negative binding affinity score and the most stable interaction with no unfavorable interactions. A zero violation of the Lipinski rule of 5 for Lobeline indicates its potential pharmacological properties. To the best of the authors' knowledge, this study represents the first in silico investigation into the properties and potential antiviral interactions of Lobeline targeting DENV4-NS1.

ACKNOWLEDGMENT

The authors express their gratitude to Nueva Ecija University of Science and Technology for their unwavering support.

Funding Sources

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Conflict of Interest

The author(s) do not have any conflict of interest.

Data Availability Statement

This statement does not apply to this article.

Ethics Statement

This research did not involve human participants, animal subjects, or any material that requires ethical approval.

Informed Consent Statement

This study did not involve human participants, and therefore, informed consent was not required.

Clinical Trial Registration

This research does not involve any clinical trials.

Permission to reproduce material from other sources

Not Applicable.

Authors' Contribution

Bautista, JJ: Conceptualization, Methodology, Data Collection and Analysis; Delos Santos, CM: Conceptualization, Methodology, Data Collection and Analysis; Teodoro, JK: Conceptualization, Methodology, Data Collection and Analysis; Duldulao, DJ: Conceptualization, Writing – Original Draft, Review & Editing, Supervision.

REFERENCES

1. Messina J.P., Brady O.J., Golding N., et al. The current and future global distribution and population at risk of dengue. *Nature Microbiology*. 2019;4(9):1508-1515.
2. Dyer O. Dengue: Philippines declares national epidemic as cases surge across South East Asia. *BMJ*. 2019;366:l5098.
3. Qaddir I, Majeed A, Hussain W, Mahmood S, Rasool N. An in silico investigation of phytochemicals as potential inhibitors against non-structural protein 1 from dengue virus 4. *Brazilian Journal of Pharmaceutical Sciences*. 2020;56.
4. Cunha MS, De Moura Coletti T, Guerra JM, et al. A fatal case of dengue hemorrhagic fever associated with dengue virus 4 (DENV-4) in Brazil: genomic and histopathological findings. *Brazilian Journal of Microbiology.* 2022;53(3):1305-1312.
5. Aryati A, Wrahatnala BJ, Yohan B, et al. Dengue virus serotype 4 is responsible for the outbreak of dengue in East Java city of Jember, Indonesia. *Viruses*. 2020;12(9):913.
6. Teixeira MG, Barreto ML. Diagnosis and management of dengue. *BMJ*. 2009;339(3):b4338.
7. Fikatas A, Vervaeke P, Meyen E, et al. A Novel Series of Indole Alkaloid Derivatives Inhibit Dengue and Zika Virus Infection by Interference with the Viral Replication Complex. *Antimicrobial Agents and Chemotherapy*. 2021;65(8).
8. Hussain G, Rasul A, Anwar H, et al. Role of plant derived alkaloids and their mechanism in neurodegenerative disorders. *International Journal of Biological Sciences*. 2018;14(3):341-357.
9. Nugraha AS, Damayanti YD, Wangchuk P, Keller PA. Anti-Infective and Anti-Cancer properties of the Annona species: their ethnomedicinal uses, alkaloid diversity, and pharmacological activities. *Molecules*. 2019;24(23):4419.
10. Zaman MAK, Azzeme AM. Plant toxins: alkaloids and their toxicities. *GSC Biological and Pharmaceutical Sciences.* 2018;6(2):021-029.
11. Daina A, Michielin O, Zoete V. SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of

small molecules. *Scientific Reports*. 2017;7(1).

12. Garg S, Roy A. In silico analysis of selected alkaloids against main protease (Mpro) of SARS-CoV-2. *Chemico-Biological Interactions*. 2020;332:109309.
13. Butt SS, Badshah Y, Shabbir M, Rafiq M. Molecular docking using Chimera and Autodock VINA software for nonbioinformaticians. *JMIR Bioinformatics and Biotechnology*. 2020;1(1):e14232.
14. Zong K, Li W, Xu Y, et al. Design, synthesis, evaluation and molecular dynamics simulation of dengue virus NS5-RDRP inhibitors. *Pharmaceuticals*. 2023;16(11):1625.
15. Liao J, Wang Q, Wu F, Huang Z. In Silico methods for identification of potential active sites of therapeutic targets. *Molecules*. 2022;27(20):7103.
16. Jendele L, Krivak R, Skoda P, Novotny M, Hoksza D. PrankWeb: a web server for ligand binding site prediction and visualization. *Nucleic Acids Research*. 2019;47(W1):W345-W349.
17. Benet LZ, Hosey CM, Ursu O, Oprea TI. BDDCS, the Rule of 5 and drugability. *Advanced Drug Delivery Reviews*. 2016;101:89-98.
18. Halder SK, Elma F. In silico identification of novel chemical compounds with antituberculosis activity for the inhibition of InhA and EthR proteins from Mycobacterium tuberculosis. *Journal of Clinical Tuberculosis and Other Mycobacterial Diseases*. 2021;24:100246.
19. Ariyanto EF, Shalannandia WA, Lantika UA, et al. Anthocyanin-Containing Purple Sweet Potato (Ipomoea batatas L.) Synbiotic Yogurt Inhibited 3T3-L1 Adipogenesis by Suppressing White Adipocyte-Specific Genes. J*ournal of Experimental Pharmacology*. 2023;Volume 15:217-230.
20. Kumar N, Kaur K, Bedi PMS. Hybridization of molecular docking studies with machine learning based QSAR model for prediction of xanthine oxidase activity. *Computational and Theoretical Chemistry*. 2023;1227:114262.