STM JOURNALS

International Journal of
Cell Biology and Cellular Functions

Volume 1, Issue 2, 2023
DOI: 10.37591/IJCBCF

https://journals.stmjournals.com/ijcbcf/

Research IJCBCF

Tinospora Sinensis Compounds for Zika Virus Targets 5JRZ and 5KVD In Silico Screening: A Potential Approach to Preventing Guillain-Barre Syndrome

Pradyum Prasad[1], Samiksha Bhor[2,*]

Abstract

Objective: *GBS is a very rare kind of disease but at the same time, it is very dangerous too. The study estimates that people who are suffering from zika virus infection are more prone to GBS. According to surveys, 1 out of 4000 people got affected by this disease, and the scariest part of this disease is that there is no cure available. In this computational era drug discovery is also done by computational methods nowadays, we choose 5JRZ and 5KVD as our target proteins to perform the molecular docking.* ***Methods:*** *The study was based on a computational approach using several types of phytocompounds for the estimation of their potential against the selected target proteins 5JRZ and 5KVD. In the process of molecular docking, different types of software and online tools will be needed to perform different types of tasks. The online tools and software are IMPPAT, PubChem, PDB, OpenBable, BIOVIA Discovery Studio, PDBsum, PyRx and Swissadme.* ***Result:*** *The molecular docking result revealed that the selected ligands have the best binding affinity with both the target proteins.* ***Conclusion:*** *The ligands could potentially be used to suppress the triggers of the GBS that will eventually treat the GBS, these findings will help researchers to find novel drugs against the GBS and Zika virus infection.*

Keywords: GBS, 5JRZ, 5KVD, *Tinospora sinensis*, molecular docking

INTRODUCTION

Guillain-Barre Syndrome is a disease that is very rare and it affects anyone at any age. It is a neurological disease in which the person's own immune system attacks the nervous system and causes muscle weakness [1]. In a worse situation, it may also be a reason for paralysis. The disease was first reported in 1916 by two physicians Georges Guillain and Jean Alexander Barre and the name of the disease was also based on the name of these two physicians [2].

The exact cause of the disease is not clear yet, but according to the studies it is found that when a viral or bacterial infection enters the body, the body's immune system got active and starts making antibodies against the infection. When these antibodies attack the body's own peripheral nervous system then the condition is called Guillain-Barre Syndrome [3]. The common bacteria and viruses are campylobacter jejuni and the zika virus against which the immune system

*Author for Correspondence
Samiksha Bhor
E-mail: SamikshaB@bionome.in

[1]Student, University Institute of Biotechnology, Chandigarh University, Punjab, India
[2]Bioinformatics Associate, Department of Biotechnology, BioNome, Bengaluru, Karnataka, India

Received Date: May 08, 2023
Accepted Date: June 02, 2023
Published Date: June 30, 2023

Citation: Pradyum Prasad, Samiksha Bhor. *Tinospora Sinensis* Compounds for Zika Virus Targets 5JRZ and 5KVD In Silico Screening: A Potential Approach to Preventing Guillain-Barre Syndrome. International Journal of Cell Biology and Cellular Functions. 2023; 1(2): 1–15p.

makes antibodies and will eventually attack the nervous system [4]. The patients who are suffering from GBS are mostly attacked by the virus zika, although it is not necessary that one who is attacked by the zika virus also develop GBS [5]. As GBS is a very rare condition but it is also true that in many cases zika may act as a trigger to develop GBS [6].

Zika virus is a mosquito-borne virus, that spreads in humans by the bite of an infected Ades mosquito [7]. Fever, joint pain, rashes over the body, and conjunctivitis is the most common symptoms but there are cases also in which one is infected by the virus and doesn't show any of the symptoms [8]. The treatment for this virus is not available yet, we only avoid this if we take proper precautions like using mosquito nets, and mosquito repellents, don't let the mosquitos bite us is the only way to avoid zika virus infection [9].

Zika virus is one of the members of the family Flaviviridae like dengue, yellow fever, and West Nile virus. The zika virus is an enclosed, single-standard RNA virus with a spherical form, like all other Flaviviridae members [10]. Three structural proteins – capsid (C), membrane(M), and envelope (E) proteins as well as non-structural proteins – NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5 – make up the virus [11]. The envelope (E) protein plays a very important role for the zika virus as it involves in the entry process and also neutralizes the antibodies whereas the NS3 non-structural protein involves in the replication process, so if we somehow find a way to inhibit at least these two proteins then we reduces the chance of getting affected by zika [12]. And if we successfully avoid the zika infection then ultimately, we don't get the GBS as we suppress the triggers.

For suppressing the triggers, we use the "giloy" plant's phytocompounds, as it is best in treating colds, headaches, fever, diarrhea, digestive issues, diabetes, and rheumatoid arthritis [13]. It belongs to the Menispermaceae family and it is a type of climbing shrub [14]. The shape of the giloy leaves was heart-shaped, the roots are Arial and had cylindrical stems. Most of the traditional medicines are prepared with the help of the stems of this plant [15]. Even the health supplements of the giloy are also available nowadays in the form of capsules, tablets, and powders [16]. If it is taken under the guidance of healthcare professionals then it will be very beneficial for our health.

And the findings also prove that the giloy is very helpful in increasing immunity and platelets which will be a great help in the treatment of dengue, a mosquito-borne disease [17]. As the giloy is useful in treating mosquito-borne diseases, we take 20 phytocompounds and try to bind them with the target proteins of zika. From this work, we try to find out the best ligand which has a good binding affinity toward the target protein.

METHODS

Retrieval of Ligands

We take 20 phytocompounds 10 of leaf and 10 of stem part of the plant *Tinospora sinensis*. The phytocompounds were retrieved from Indian Medicinal Plants, Phytochemistry and Therapeutics 2.0 (IMPPAT 2.0), the official website for the IMPPAT is https://cb.imsc.res.in/imppat/home. The canonical SMILES, PubChem CID, and chemical structure in 3D SDF format were retrieved from the database named PubChem (https://pubchem.ncbi.nlm.nih.gov/). After that, all 3D SDF files will be converted to PDB file format using the software Open-Babel for docking purposes [18].

ADME Analysis

For analyzing the adme properties of the molecule we use SwissADME online tool (http://www.swissadme.ch/index.php). There we analyze the druglikeness properties in which we see whether it follows the Lipinski rule of five or not if any molecule has three or more Lipinski violations then the particular molecule will not be taken further for the docking [19].

Protein Retrieval and Purification

The three-dimensional (3D) structure of protein NS3 Helicase (5JRZ) and envelope protein (5KVD) was resolved using the X-ray diffraction method with a resolution of 1.62Å and 1.65Å respectively. The 3D structures of the proteins were downloaded from the Research Collaboratory for Structural Bioinformatics PDB (RCSB PDB) in pdb format. The official website of the RCSB PDB is https://www.rcsb.org/. Using Biovia Discovery Studio, clean the protein that is keeping the main chains and delete the rest of the chains, heteroatoms, and other molecules which is not required, then save the cleaned structure in the pdb file format. We can also generate the hydropathy plots using Biovia Discovery Studio. Use the cleaned structure on PDBsum (http://www.ebi.ac.uk/thornton-srv/databases/pdbsum/) to obtain their 2-dimensional structure and Ramachandran plot.

Molecular Docking

Once the ligand and protein were retrieved and the cleaning of the protein was also done then the next step is molecular docking. We use PyRx software for doing the docking as it is basically a computational molecular screening tool that allows us to make macromolecules and also added the AutoDock Vina feature to perform the molecular docking. Here we use 20 phytocompounds as ligands and there are 2 target proteins named 5JRZ & 5KVD. After loading the target protein convert it into a macromolecule. Then on the open babel tool available on PyRx, load all the ligands do energy minimization of all the ligands and then convert all to AutoDock ligands (pdbqt). And for target proteins, the grid was generated Table:1 shows the grid details.

Table 1. Grid center of target proteins.

PDB ID of the target protein	X	Y	Z
5JRZ	35.5544	25.707	37.9378
5KVD	-3.1803	12.9001	-18.2575

All the ligands will be docked with the target proteins and we get the result in the form of a table that has a binding affinity and RMSD. The lesser the value of binding affinity means the best the docking conformation is [20], we take the top 3 ligands which have the least binding affinity value and zero RMSD value.

Visualization

The top three ligands having the least binding affinity for each protein will be selected and then we save the docked ligand in pdb format from PyRx. Then we simply show the interaction or visualize the protein-ligand interaction on BIOVIA Discovery Studio and save the visuals in png format.

RESULTS

Selection of Phytocompounds

We retrieved 20 phytocompounds of the plant *Tinospora sinensis* from IMPPAT, in Table 2 we mentioned the canonical smiles of the retrieved molecules from PubcChem for the docking and based on the result we got from the swissadme we select the phytocompounds suitable for docking.

SwissADME

Adme analysis

Out of 20 phytocompounds 1 got rejected and 19 were selected for the docking procedure as only one compound has 3 Lipinski violations. Swissadme gives the result under different parameters like Physicochemical Properties, Lipophilicity, Water solubility, Pharmacokinetics, Druglikeness, and Medicinal chemistry. In this work, we mainly focus on three categories Physicochemical Properties, Pharmacokinetics, and Druglikeness (Tables 3–6).

Table 2. Molecules and it's canonical smiles.

Molecule	Canonical SMILES
Myristic acid	CCCCCCCCCCCCCC(=O)O
Heptacosane	CCCCCCCCCCCCCCCCCCCCCCCCCCC
1-Penten-3-OL	CCC(C=C)O
Pentadecanoic acid	CCCCCCCCCCCCCCC(=O)O
Nonanal	CCCCCCCCC=O
2-Penten-1-OL	CC/C=C/CO
1-Heptacosanol	CCCCCCCCCCCCCCCCCCCCCCCCCCCO
Hydroquinone	Oc1ccc(cc1)O
1-Octacosanol	CCCCCCCCCCCCCCCCCCCCCCCCCCCCO
1-Hexanol	CCCCCCO
Xanosporic acid	COc1c(CC(O)C)c2c3c(CC(O)C)c(oc4c3c3c5c2c(c1O)c(=O)cc5OCOc3cc4O)C(=O)O
Cordifolide A	OC[C@H]1O[C@@H](OCCS[C@H]2CC[C@@H]3[C@@]4([C@@]2(O)C(=O)O[C@H]4C[C@@H]2[C@@]3(C)C[C@H](OC2=O)c2cocc2)C)[C@@H]([C@H]([C@@H]1O)O)O
Tinosponone	O=C1O[C@@H](C[C@@]2([C@H]1CC[C@@]1([C@H]2C(=O)C=C[C@H]1O)C)C)c1cocc1
Tinosporaside	OC[C@H]1O[C@@H](O[C@@H]2C=CC(=O)[C@@H]3[C@@]2(C)CC[C@@H]2[C@@]3(C)C[C@H](OC2=O)c2cocc2)[C@@H]([C@H]([C@@H]1O)O)O
Tinosporinone	COc1ccc(c(c1)OC)C(=O)C(C(=O)c1ccc2c(c1)OCO2)C
Malabarolide	O[C@@H]1C[C@H](O)C2[C@H]([C@@H]1O)C1(C)C[C@@H](OC(=O)C1(CC2)O)c1cocc1
Kaempferol	Oc1ccc(cc1)c1oc2cc(O)cc(c2c(=O)c1O)O
Tembetarine	COc1ccc(cc1O)C[C@H]1c2cc(O)c(cc2CC[N+]1(C)C)OC
Berberine	COc1c(OC)ccc2c1c[n+]1CCc3c(c1c2)cc1c(c3)OCO1

Table 3. Physicochemical properties of top 3 phytocompounds.

Molecule	Formula	MW	#Heavy atoms	#Aromatic heavy atoms	Fraction Csp3	#Rotatable bonds	#H-bond acceptors	#H-bond donors	MR	TPSA
Myristic acid	$C_{14}H_{28}O_2$	228.37	16	0	0.93	12	2	1	71.18	37.3
Heptacosane	$C_{27}H_{56}$	380.73	27	0	1	24	0	0	131.9	0
1-Penten-3-OL	$C_5H_{10}O$	86.13	6	0	0.6	2	1	1	26.84	20.23
Pentadecanoic acid	$C_{15}H_{30}O_2$	242.4	17	0	0.93	13	2	1	75.99	37.3
Nonanal	$C_9H_{18}O$	142.24	10	0	0.89	7	1	0	45.58	17.07
2-Penten-1-OL	$C_5H_{10}O$	86.13	6	0	0.6	2	1	1	26.84	20.23
1-Heptacosanol	$C_{27}H_{56}O$	396.73	28	0	1	25	1	1	133.06	20.23
Hydroquinone	$C_6H_6O_2$	110.11	8	6	0	0	2	2	30.49	40.46
1-Octacosanol	$C_{28}H_{58}O$	410.76	29	0	1	26	1	1	137.87	20.23
1-Hexanol	$C_6H_{14}O$	102.17	7	0	1	4	1	1	32.12	20.23
Xanosporic acid	$C_{28}H_{24}O_{11}$	536.48	39	20	0.29	6	11	5	141.23	176.12
Cordifolide A	$C_{28}H_{38}O_{12}S$	598.66	41	5	0.79	7	12	5	141.32	210.65
Tinosponone	$C_{19}H_{22}O_5$	330.37	24	5	0.58	1	5	1	86.28	76.74
Tinosporaside	$C_{25}H_{32}O_{10}$	492.52	35	5	0.68	4	10	4	118.67	155.89
Tinosporinone	$C_{19}H_{18}O_6$	342.34	25	12	0.26	6	6	0	90.21	71.06
Malabarolide	$C_{18}H_{24}O_7$	352.38	25	5	0.72	1	7	4	85.53	120.36
Kaempferol	$C_{15}H_{10}O_6$	286.24	21	16	0	1	6	4	76.01	111.13
Tembetarine	$C_{20}H_{26}NO_4^+$	344.42	25	12	0.4	4	4	2	102.87	58.92
Berberine	$C_{20}H_{18}NO_4^+$	336.36	25	16	0.25	2	4	0	94.87	40.8

Table 4. Pharmacokinetics

Molecule	GI absorption	BBB permeant	Pgp substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	log Kp (cm/s)
Myristic acid	High	Yes	No	Yes	No	No	No	No	-3.35
Heptacosane	Low	No	Yes	No	No	No	No	No	1.49
1-Penten-3-OL	High	Yes	No	No	No	No	No	No	-6.04
Pentadecanoic acid	High	Yes	No	Yes	No	Yes	No	No	-3.07
Nonanal	High	Yes	No	No	No	No	No	No	-4.85
2-Penten-1-OL	High	Yes	No	No	No	No	No	No	-6.22
1-Heptacosanol	Low	No	Yes	No	No	No	No	No	0.56
Hydroquinone	High	Yes	No	No	No	No	No	Yes	-6.55
1-Octacosanol	Low	No	Yes	No	No	No	No	No	0.86
1-Hexanol	High	Yes	No	No	No	No	No	No	-5.48
Xanosporic acid	Low	No	No	No	No	Yes	No	No	-7.31
Cordifolide A	Low	No	Yes	No	No	No	No	No	-9.7
Tinosponone	High	Yes	Yes	No	No	No	No	No	-7.01
Tinosporaside	Low	No	Yes	No	No	No	No	No	-9.13
Tinosporinone	High	Yes	No	Yes	Yes	Yes	Yes	Yes	-5.95
Malabarolide	High	No	Yes	No	No	No	No	No	-8.46
Kaempferol	High	No	No	Yes	No	No	Yes	Yes	-6.7
Tembetarine	High	Yes	Yes	No	No	No	Yes	Yes	-6.25
Berberine	High	Yes	Yes	Yes	No	No	Yes	Yes	-5.78

Table 5. Druglikeness.

Molecule	Lipinski #violations	Ghose #violations	Veber #violations	Egan #violations	Muegge #violations	Bioavailability Score
Myristic acid	0	0	1	0	1	0.85
Heptacosane	1	3	1	1	3	0.55
1-Penten-3-OL	0	3	0	0	2	0.55
Pentadecanoic acid	0	0	1	0	1	0.85
Nonanal	0	1	0	0	2	0.55
2-Penten-1-OL	0	3	0	0	2	0.55
1-Heptacosanol	1	3	1	1	3	0.55
Hydroquinone	0	3	0	0	1	0.55
1-Octacosanol	1	3	1	1	3	0.55
1-Hexanol	0	2	0	0	2	0.55
Xanosporic acid	2	2	1	1	2	0.11
Cordifolide A	2	3	1	1	2	0.17
Tinosponone	0	0	0	0	0	0.55
Tinosporaside	0	1	1	1	1	0.55
Tinosporinone	0	0	0	0	0	0.55
Malabarolide	0	0	0	0	0	0.55
Kaempferol	0	0	0	0	0	0.55
Tembetarine	0	0	0	0	0	0.55
Berberine	0	0	0	0	0	0.55

Table 6. Molecule showing 3 Lipinski violations.

Molecule	Lipinski #violations	Ghose #violations	Veber #violations	Egan #violations	Muegge #violations	Bioavailability Score
Tinosinen	3	2	1	1	3	0.17

As Tinosinen showing 3 Lipinski violations, so it will not take further for docking. Hence only 19 phytocompounds should be taken for molecular docking. In Figure 1, the selected 19 compounds will be shown.

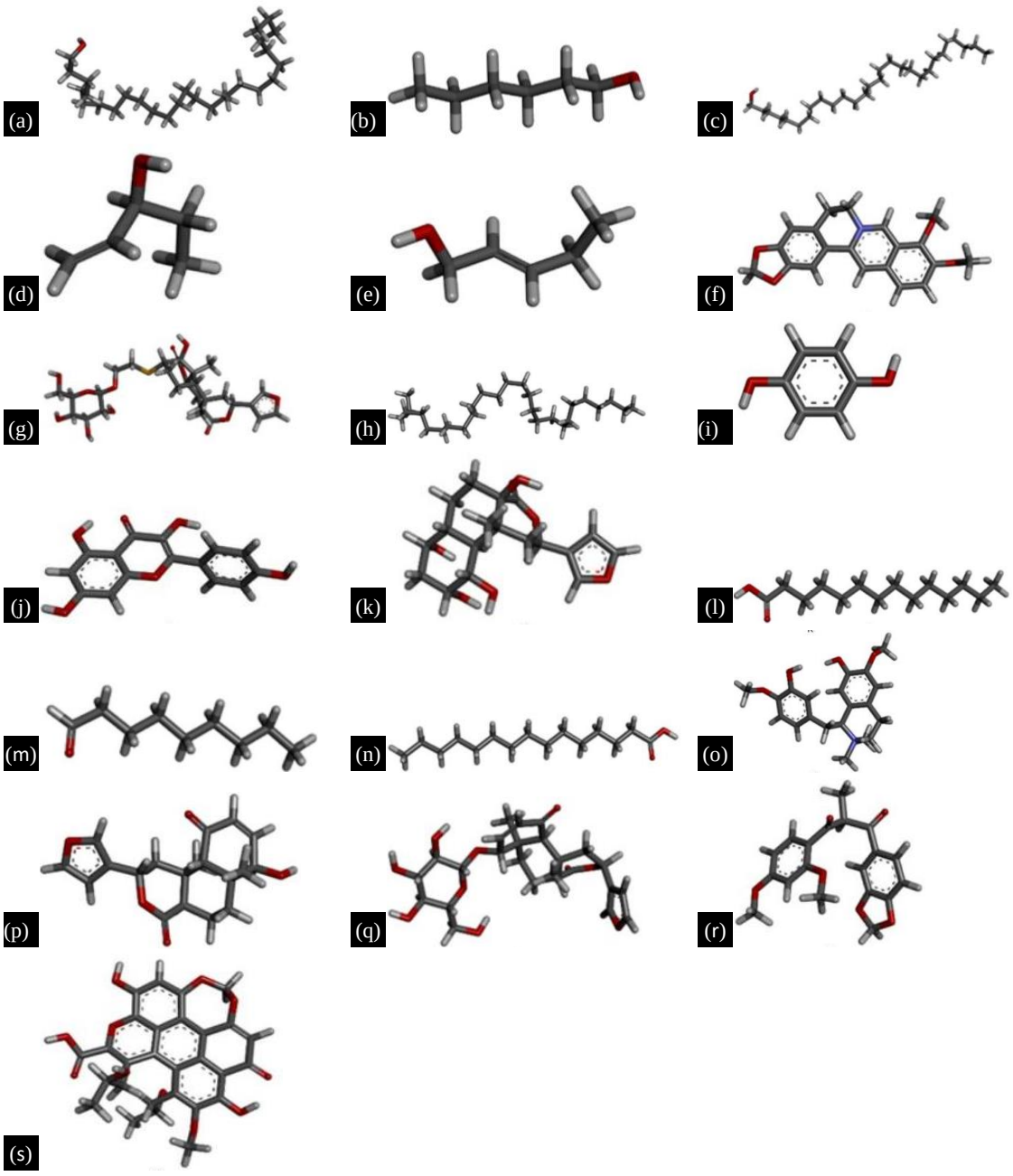


Figure 1. Structure of 19 selected phytocompounds of plant *Tinospora sinensis*, {(a) 1-Heptacosanol, (b) 1-Hexanol, (c) 1-Octacosanol, (d) 1-Penten-3-OL, (e) 2-Penten-1-OL, (f) Berberine, (g) Cordifolide A, (h) Heptacosane, (i) Hydroquinone, (j) Kaempferol, (k) Malabarolide, (l) Myristic acid, (m) Nonanal, (n) Pentadecanoic acid, (o) Tembetarine, (p) Tinosponone, (q) Tinosporaside, (r) Tinosporinone, (s) Xanosporic acid}

Protein Retrieval and Purification

We download the three-dimensional structure of the target proteins in pdb format from RCSB-PDB. Then we open the downloaded structure in Biovia Discovery Studio for the purification process. The purified three-dimensional structure of the protein is shown in Figures 2 and 3. And for structural analysis Ramachandran-plot, Secondary structure, and Hydrophobicity-plot were analyzed.

5JRZ – it is a NS3 helicase of the zika virus, and we used it as a receptor.

- *Ramachandran-Plot:* As shown in Figure 3; 5JRZ has 92.3% of the residues in the area which is claimed to be the most preferred regions and 7.7% are in the extra allowed regions.
- *Hydrophobicity:* from BIOVIA Discovery Studio we getting this plot which helps us in the structural analysis of target protein (Figure 4).

- *Secondary structure:* we use pdbsum for predicting the secondary structure of 5JRZ and we get 5 sheets, 2 beta alpha beta units, 3 beta hairpins, 2 beta bulges, 18 strands, 20 helices, 17 helix-helix interacs, 34 beta turns, and 4 gamma turns (Figure 5).

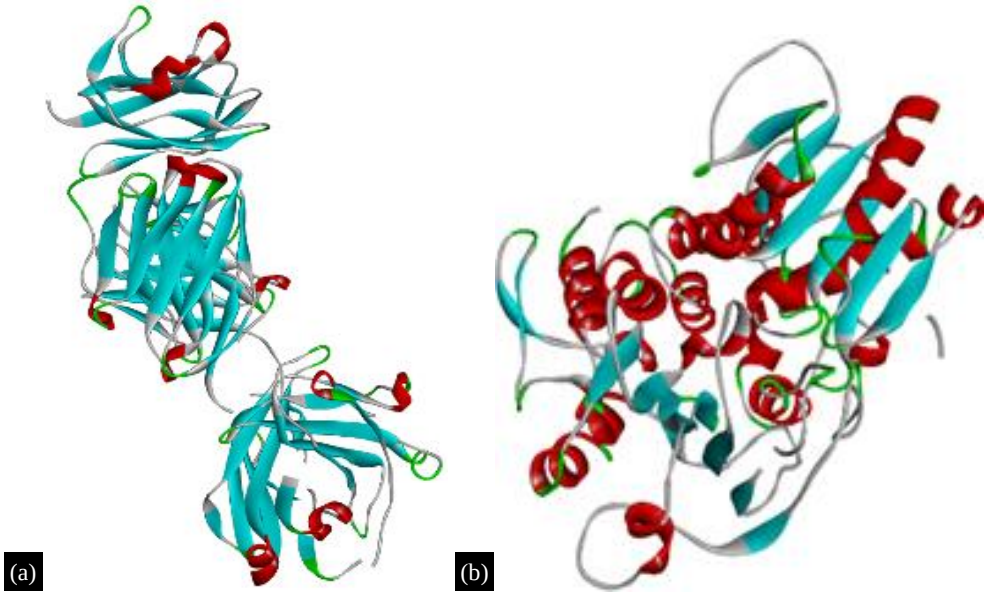
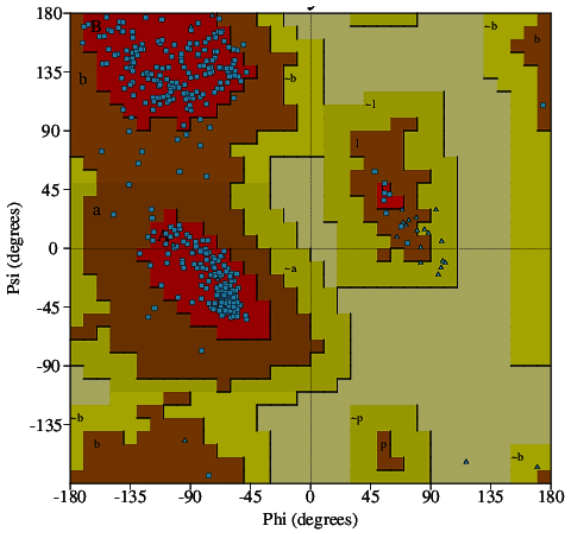


Figure 2. Cleaned 3D structure of (a) 5KVD & (b) 5JRZ.



1. Ramachandran Plot statistics

		No. of residues	%-tage
Most favoured regions	[A,B,L]	347	92.3%
Additional allowed regions	[a,b,l,p]	29	7.7%
Generously allowed regions	[~a,~b,~l,~p]	0	0.0%
Disallowed regions	[XX]	0	0.0%
Non-glycine and non-proline residues		376	100.0%
End-residues (excl. Gly and Pro)		11	
Glycine residues		27	
Proline residues		24	
Total number of residues		438	

Figure 3. Ramachandran plot and plot statistics of 5JRZ.

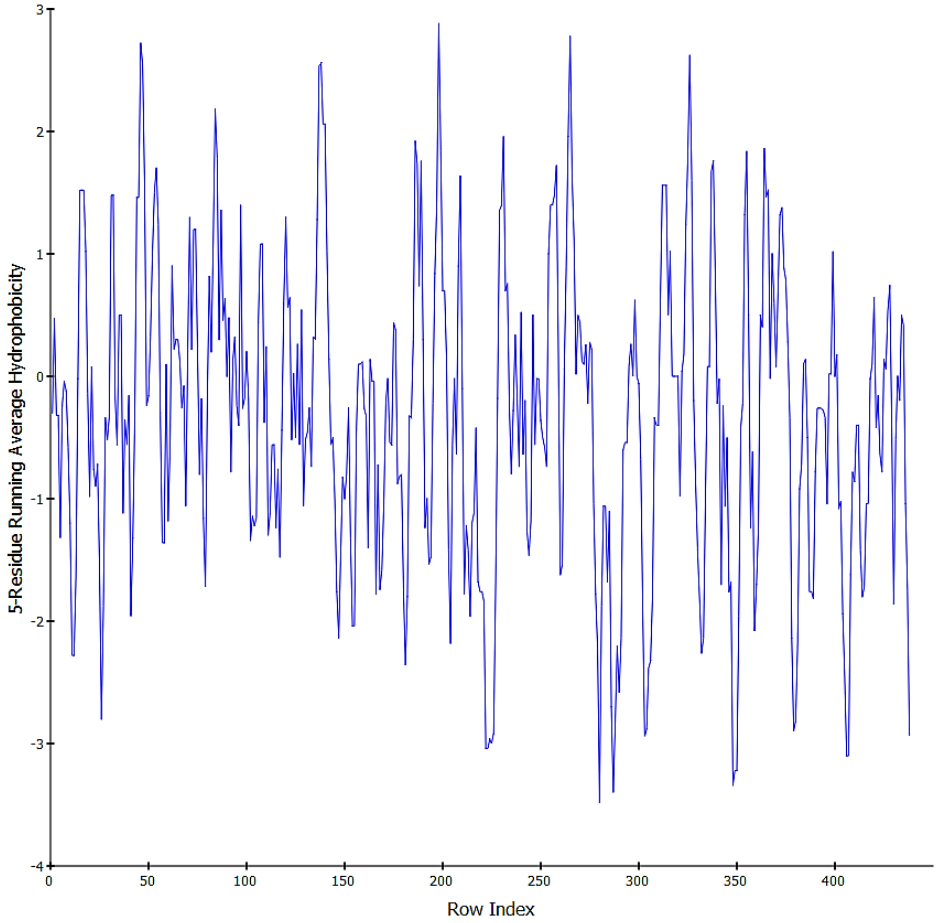


Figure 4. Hydrophobicity chart of 5JRZ.

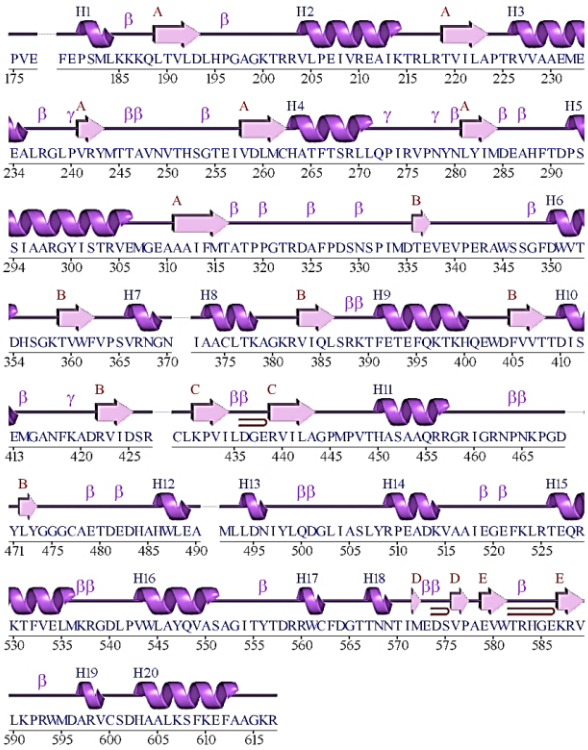
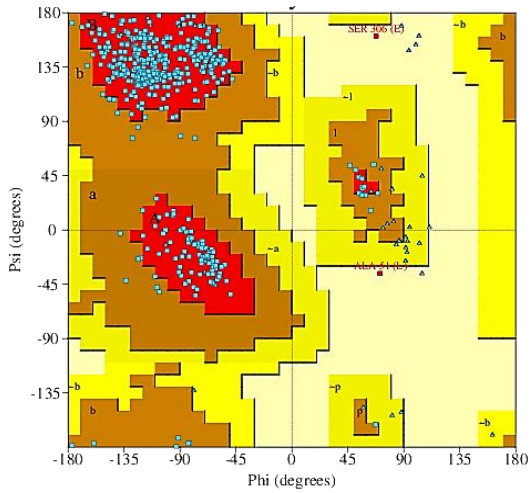


Figure 5. Secondary structure of 5JRZ.

5KVD: It is an envelope protein of the zika virus and we choose is as a target protein for our docking.

- *Ramachandran-Plot:* As shown in Figure 6; 5KVD has 92.9% of the residues in the area which is claimed to be the most preferred regions and 6.6% are in the extra allowed regions.
- *Hydrophobicity:* from BIOVIA Discovery Studio we getting this plot which helps us in the structural analysis of target protein (Figure 7).



1. Ramachandran Plot statistics

		No. of residues	%-tage
Most favoured regions	[A,B,L]	408	92.9%
Additional allowed regions	[a,b,l,p]	29	6.6%
Generously allowed regions	[~a,~b,~l,~p]	0	0.0%
Disallowed regions	[XX]	2	0.5%*
Non-glycine and non-proline residues		439	100.0%
End-residues (excl. Gly and Pro)		24	
Glycine residues		44	
Proline residues		30	
Total number of residues		537	

Figure 6. Ramachandran plot and plot statistics of 5KVD.

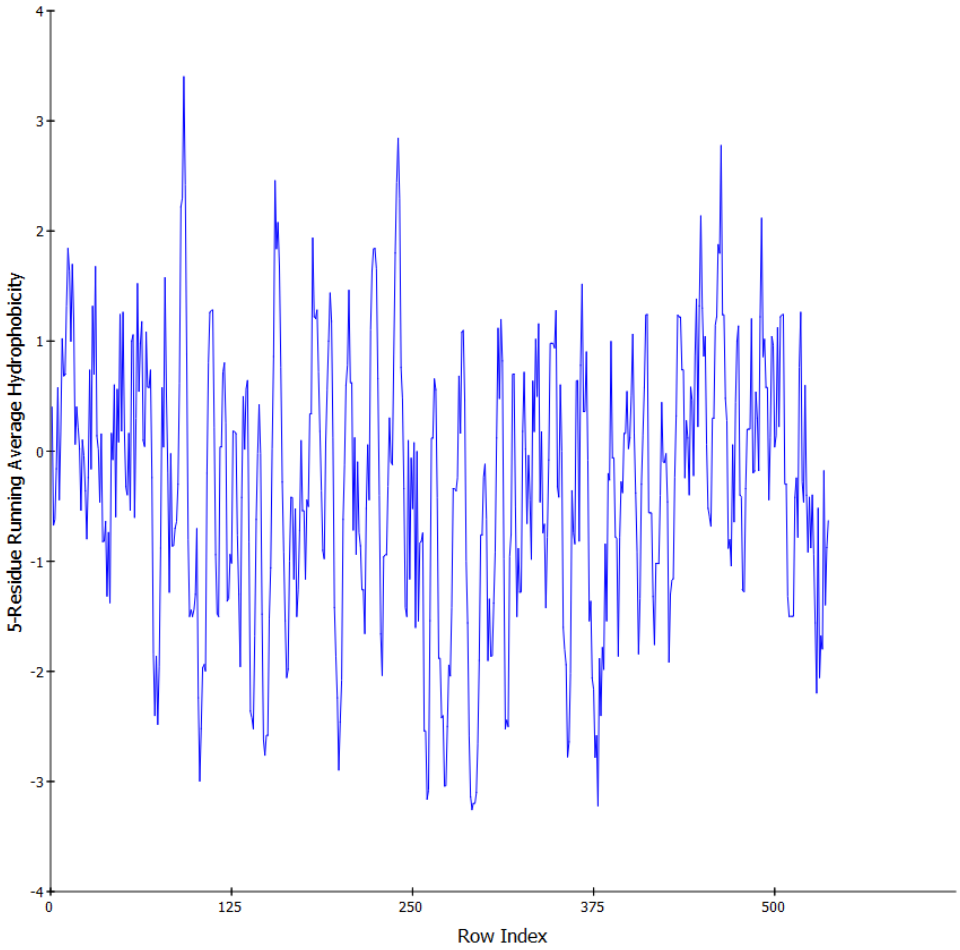


Figure 7. Hydrophobicity chart of 5KVD.

- *Secondary structure:* the predicted secondary structure consists of three chains E, H and L. Chain E contains 3 sheets, 2 beta hairpins, 2 beta bulges, 10 strands, 2 helices, 7 beta turns, 1 gamma turn, and 1 disulphide. Chain H has 4 sheets, 7 beta hairpins, 4 beta bulges, 18 strands, 6 helices, 18 beta turns, 1 gamma turn, and 2 disulphides whereas Chain L has 5 sheets, 7 beta hairpins, 4 beta bulges, 18 strands, 3 helices, 1 helix-helix interac, 21 beta turns, 2 gamma turns, and 2 disulphides (Figures 8–10).

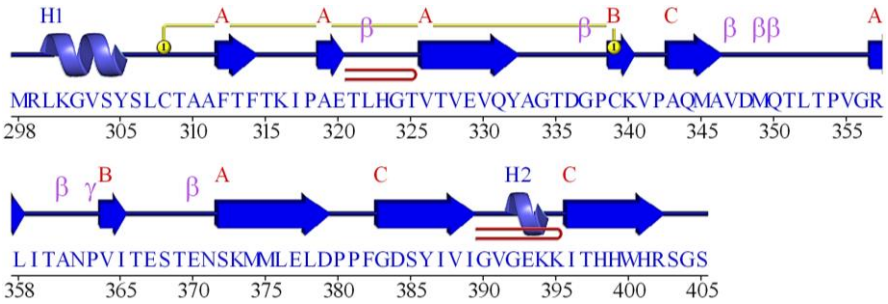


Figure 8. Secondary structure of 5KVD (Chani E).

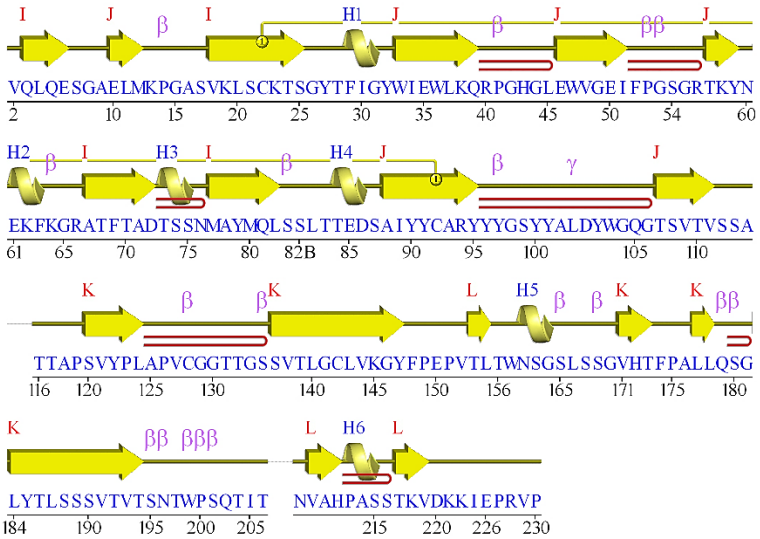


Figure 9. Secondary structure of 5KVD (Chani H).

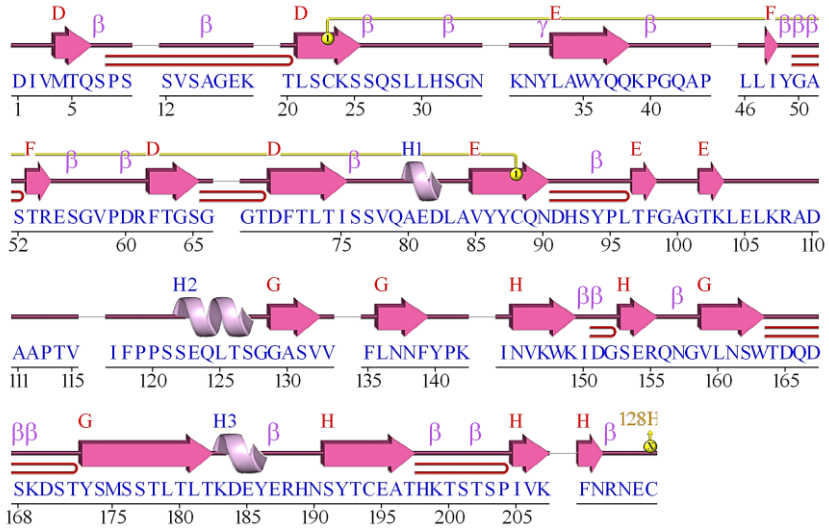


Figure 10. Secondary structure of 5KVD (Chani L).

Molecular Docking

Twenty compounds were retrieved from the IMPPAT out of which 19 compounds are selected for the docking. After the docking was done and we get the result, we analyze the result and find the top 3 compounds which shows the lowest binding affinity and zero RMSD value. In Table 7 we show the top 3 compounds whose binding affinity is the lowest, which we get as a result of the docking using PyRx software

Table 7. Top 3 compounds showing least binding affinity for 5JRZ & 5KVD.

Ligand	Binding Affinity	RMSD
5jrz_Berberine_uff_E=579.71	-8.2	0
5jrz_Cordifolide_uff_E=1155.34	-8.9	0
5jrz_Tinosporaside_uff_E=818.13	-8.2	0
5kvd_Berberine_uff_E=579.71	-7.6	0
5kvd_Cordifolide_uff_E=1155.34	-8.6	0
5kvd_Tinosporaside_uff_E=818.13	-7.6	0

Visualization

Then we visualize the receptor-ligand interaction using the Biovia Discovery Studio. (Figure 11)

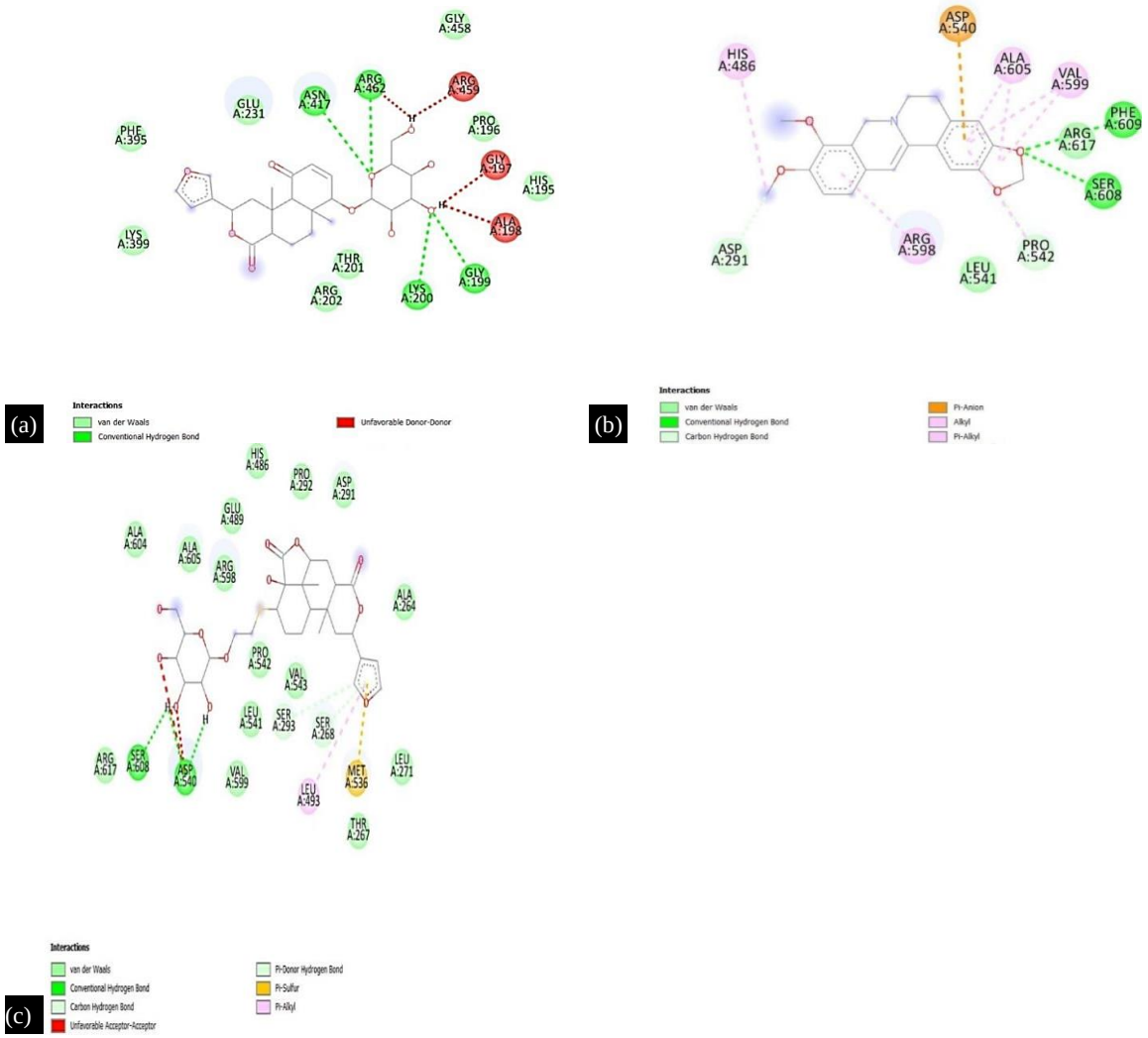


Figure 11. Top 3 ligand interaction with 5JRZ (a) 5jrz_Tinosporasid (b) 5jrz_Berberine (c) 5jrz_Cordifolide.

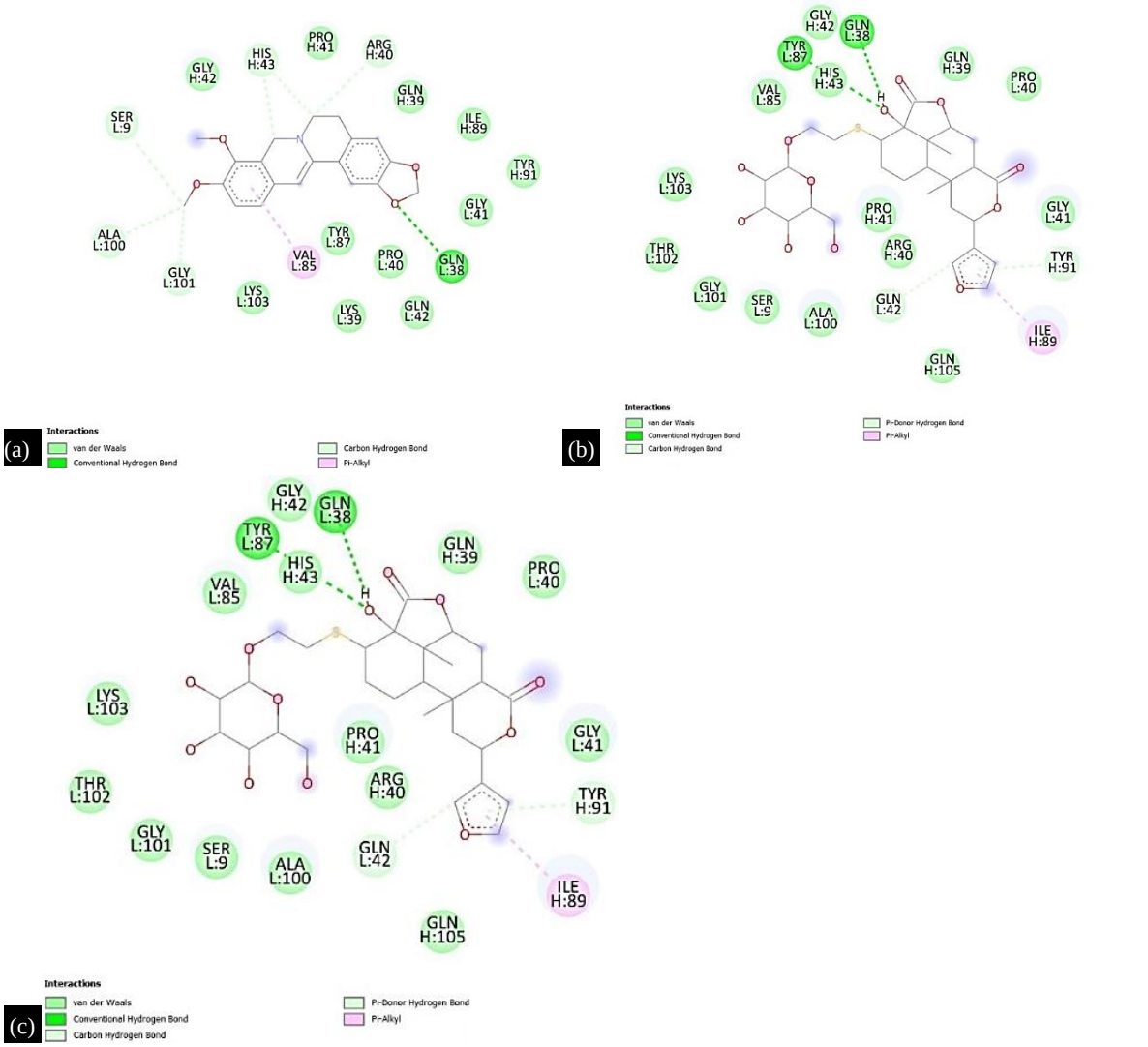


Figure 12. Top 3 ligand interaction with 5KVD (a) 5kvd_Berberine (b) 5kvd_Cordifolide (c) 5kvd_Tinosporaside.

From the above visualization (Figure 12) we get to know about the interactions between the ligands and the receptor.

DISCUSSION

As we know that the Guillain-Barre syndrome is an autoimmune disease which is very rare, it is a kind of disorder which usually occur when it got triggers, for example when a virus, pathogen or bacteria attacks to the body then the body make antibodies against it in order to fight with the pathogens but sometimes somehow these antibodies starts attacking the body's own nerve cell outside the brain and spinal cord which causes muscle weakness, numbness or even cause paralysis in worst scenarios [21]. Hence, GBS is a very rare but dangerous disorder.

The exact cause of GBS is still unknown, but according to studies it is believed to be triggered by an infection, such as viral or bacterial [22]. And according to researchers in many cases, the Zika virus is proven to be a trigger for GBS [23]. Areas which has an outbreak of the Zika virus, report an increment in the cases of GBS [24]. The Centers for Disease Control and Prevention (CDC) reports that according to some studies it is found that up to 1 in 4000 people infected with the Zika virus may develop GBS [25].

Zika virus is a viral infection that spreads in humans through the bite of an infected mosquito. The general symptoms of zika infection are fever, rash, joint pain, and conjunctivitis but sometimes many infected persons don't even develop a single symptom [26]. Zika infection is also very difficult to treat and the best way to protect against Zika is the prevention till date [27]. As zika is a mosquito-borne disease and according to studies it is proven how important the Giloy plant is in order to treat mosquito-borne diseases like dengue [28]. As giloy has many medicinal properties like anti-inflammatory properties, and antioxidant properties, boosts immunity, and has a quality to improve the condition of fever, so here we trying to find the best phytocompound which binds to the target and suppresses the infection [29].

The target protein of the Zika virus is the envelope protein (E protein), which is responsible for the entry of the virus or infection [30]. The E protein of the virus gets attached to the host cells receptor which leads to the fusion of the virus and host cell and promotes replication resulting in an increasing number of viral cells in the host [31]. So, in order to suppress the effect of zika E protein will be the best target for the development of vaccines or antiviral drugs [32]. We take 5JRZ the crystal structure of the Zika virus envelope protein and 5KVD the crystal structure of the full-length Zika virus NS5 protein, as these proteins plays important role in viral replication and immune evasion so these two will be the perfect candidate to become our target proteins for the molecular docking [33].

Once we find the best ligand which binds to our receptors then we are able to suppress the effect of triggers and when the trigger suppresses the GBS will not going to happen [34]. And if the GBS already occurred then we use our docked product to neutralize the effect of triggers and then GBS will be treated with the help of Immunotherapy, Rehabilitation, Supportive care, and managing the pain of the patients also be a measure to decrease down the effect of GBS [35].

Currently, there is no perfect cure for Zika as well as GBS (Guillain-Barre Syndrome) [36, 37] and present treatment will improve the conditions by simply minimizing the effects it does not work on the target point of the disease which is why it takes a long time to treat the diseases. So, our work might help the researchers in finding a cure for this rare but deadly disease.

In this paper, we get to know about the disease Guillain-Barre Syndrome as it is an autoimmune disease that damages the nerves of the brain or spinal cord and leads the paralysis like dangerous condition. The exact cause is still unknown but we get to know that it will be triggered by some types of viral or bacterial infections. And we decided to take a disease that triggers the GBS most and the disease or infection is Zika virus infection. The zika virus infection is a mosquito-borne disease and its cure is also not available so, we try to find out the best ligand which binds with the receptors and suppresses the replication of the virus in the host's body and not allows to spread of the infection. So, by this finding, we can also suppress the GBS. From studies, we find that the Giloy plant is very beneficial and has great medicinal properties in them which allow the plant to be the best candidate in order to find a cure for GBS. As we have already seen the effect of giloy on mosquito-borne diseases like dengue we try to dock some of the phytocompounds of the plant to the target proteins of the disease. And we get some best phytocompounds that have the lowest binding affinity with the target proteins which proves that the Giloy plant will be effective in order to cure the disease.

Acknowledgement

I would like to thank Ms. Samiksha Bhor for her guidance in undertaking the current project. I thank BioNome (https://bionome.in/) for offering computational facilities and support in scientific research services.

Abbreviation

ADME analysis	Absorption Digestion Metabolism Excretion analysis
GBS	Guillain-Barre Syndrome
IMPPAT	Indian Medicinal Plants, Phytochemistry and Therapeutics

REFERENCES

1. Willison, H. J., Jacobs, B. C., & van Doorn, P. A. (2016). Guillain-barre syndrome. *The Lancet*, *388*(10045), 717–727.
2. Hughes, R. A., & Cornblath, D. R. (2005). Guillain-barre syndrome. The Lancet, 366(9497), 1653-1666.
3. Shahrizaila, N., Lehmann, H. C., & Kuwabara, S. (2021). Guillain-Barré syndrome. The lancet, 397(10280), 1214–1228.
4. Laman, J. D., Huizinga, R., Boons, G. J., & Jacobs, B. C. (2022). Guillain-Barré syndrome: expanding the concept of molecular mimicry. Trends in immunology.
5. Das, M. P. Molecular Docking Studies of Compounds from Euphorbia Hirta and Bacopa Monnieri To ZIKA Virus Structural and Non Structural Proteins.
6. Meewan, I., Shiryaev, S., Huang, C. T., Lin, Y. W., Chuang, C. H., Terskikh, A., & Abagyan, R. (2022). Allosteric inhibitors of Zika virus NS2B-NS3 protease targeting protease in super-open conformation. bioRxiv, 2022–03.
7. Jalal, K., Khan, K., Hayat, A., Ahmad, D., Alotaibi, G., Uddin, R., ... & Basharat, Z. (2022). Mining therapeutic targets from the antibiotic-resistant Campylobacter coli and virtual screening of natural product inhibitors against its riboflavin synthase. Molecular Diversity, 1-18.
8. Kumar, A., Kumar, D., Kumar, P., Jones, B. L., Mysorekar, I. U., & Giri, R. (2022). Discovery And Characterization of Small Molecule Inhibitors of Zika Virus Replication. bioRxiv, 2022–12.
9. Fong, Y. D., & Chu, J. J. H. (2022). Natural products as Zika antivirals. Medicinal Research Reviews, 42(5), 1739–1780.
10. Ullah, S., Zheng, Z., Li, Y., Rahman, W., Ullah, F., Ullah, A., ... & Gao, T. Inhibition of Zika Virus NS2B-NS3 Viral Protease by Tripeptide Inhibitor Using Molecular Docking and Molecular Dynamics Simulations. Available at SSRN 4188641.
11. Cruz-Arreola, O., Orduña-Diaz, A., Domínguez, F., Reyes-Leyva, J., Vallejo-Ruiz, V., Domínguez-Ramírez, L., & Santos-López, G. (2022). In silico testing of flavonoids as potential inhibitors of protease and helicase domains of dengue and Zika viruses. *PeerJ*, *10*, e13650.
12. Qian, W., Zhou, G. F., Ge, X., Xue, J. X., Zheng, C. B., Yang, L. M., ... & Zhou, G. C. (2022). Discovery of dehydroandrographolide derivatives with C19 hindered ether as potent anti-ZIKV agents with inhibitory activities to MTase of ZIKV NS5. *European Journal of Medicinal Chemistry*, *243*, 114710.
13. Trivedi, N., Mishra, A., & Kumar, D. (2022). Herbal medicine is the way of potential therapeutic option for the treatment of COVID-19: Recent updates. Journal of Complementary Medicine Research, 13(1), 27-27.
14. Sharma, D., Sharma, N., Manchanda, N., Prasad, S. K., Sharma, P. C., Thakur, V. K., ... & Dhobi, M. (2022). Bioactivity and In Silico Studies of Isoquinoline and Related Alkaloids as Promising Antiviral Agents: An Insight. Biomolecules, 13(1), 17.
15. Mohsin, A., & Bhandari, K. (2022, March). Molecular docking studies to find a natural inhibitor against dengue. In AIP Conference Proceedings (Vol. 2424, No. 1, p. 060006). AIP Publishing LLC.
16. Sarkar, D., Goswami, R., Sarkar, A., & Mukherjee, S. (2022). role of tinospora cordifolia (giloy) in bone maintenance disorder (osteoporosis) by docking analytical study. *epra International Journal of Research and Development (IJRD)*, *7*(4), 1–8.
17. Taslem Mourosi, J., Awe, A., Jain, S., & Batra, H. (2022). Nucleic Acid Vaccine Platform for DENGUE and ZIKA Flaviviruses. *Vaccines*, *10*(6), 834.
18. Molla, M. H. R., Aljahdali, M. O., Sumon, M. A. A., Asseri, A. H., Altayb, H. N., Islam, M., ... & Mohammad, F. (2023). Integrative Ligand-Based Pharmacophore Modeling, Virtual Screening, and Molecular Docking Simulation Approaches Identified Potential Lead Compounds against Pancreatic Cancer by Targeting FAK1. *Pharmaceuticals*, *16*(1), 120.
19. Azzam, K. A. (2023). SwissADME and pkCSM Webservers Predictors: an integrated Online Platform for Accurate and Comprehensive Predictions for In Silico ADME/T Properties of Artemisinin and its Derivatives. *Kompleksnoe Ispolzovanie Mineralnogo Syra*, *325*(2), 14–21.

20. Crampon, K., Giorkallos, A., Deldossi, M., Baud, S., & Steffenel, L. A. (2022). Machine-learning methods for ligand–protein molecular docking. *Drug discovery today*, *27*(1), 151–164.
21. van Doorn, P. A. (2013). Diagnosis, treatment and prognosis of Guillain-Barré syndrome (GBS). *La Presse Médicale*, *42*(6), e193-e201.
22. Marcus, R. (2023). What Is Guillain-Barré Syndrome?. *JAMA*, *329*(7), 602-602.
23. Davies, A. J., Lleixà, C., Siles, A. M., Gourlay, D. S., Berridge, G., Dejnirattisai, W., ... & Rinaldi, S. (2023). Guillain-Barré syndrome following Zika virus infection is associated with a diverse spectrum of peripheral nerve reactive antibodies. *Neurology-Neuroimmunology Neuroinflammation*, *10*(1).
24. Lazarini, F., Lannuzel, A., Cabié, A., Michel, V., Madec, Y., Chaumont, H., ... & Ungeheuer, M. N. (2022). Olfactory outcomes in Zika virus-associated Guillain–Barré syndrome. *European Journal of Neurology*, *29*(9), 2823–2831.
25. Lunn, M. P. (2022). Guillain-Barré syndrome in an era of global infections and 21st century vaccination. *Current Opinion in Neurology*, *35*(5), 571-578.
26. Basarab, M., Bowman, C., Aarons, E. J., & Cropley, I. (2016). Zika virus. *Bmj*, *352*.
27. Chen, H. L., & Tang, R. B. (2016). Why Zika virus infection has become a public health concern?. *Journal of the Chinese Medical Association*, *79*(4), 174–178.
28. Sarangi, M. K., & Soni, S. (2013). A review on giloy: the magic herb. *Inventi Rapid: Planta Activa*, *2*, 1–4.
29. Shree, P., Mishra, P., Selvaraj, C., Singh, S. K., Chaube, R., Garg, N., & Tripathi, Y. B. (2022). Targeting COVID-19 (SARS-CoV-2) main protease through active phytochemicals of ayurvedic medicinal plants–Withania somnifera (Ashwagandha), Tinospora cordifolia (Giloy) and Ocimum sanctum (Tulsi)–a molecular docking study. *Journal of Biomolecular Structure and Dynamics*, *40*(1), 190–203.
30. Priya, S., Kumar, N. S., & Hemalatha, S. (2018). Antiviral phytocompounds target envelop protein to control Zika virus. *Computational Biology and Chemistry*, *77*, 402–412.
31. Kang, C., Keller, T. H., & Luo, D. (2017). Zika virus protease: an antiviral drug target. *Trends in microbiology*, *25*(10), 797–808.
32. Gratton, R., Agrelli, A., Tricarico, P. M., Brandão, L., & Crovella, S. (2019). Autophagy in Zika virus infection: a possible therapeutic target to counteract viral replication. *International journal of molecular sciences*, *20*(5), 1048.
33. Panayiotou, C., Lindqvist, R., Kurhade, C., Vonderstein, K., Pasto, J., Edlund, K., ... & Överby, A. K. (2018). Viperin restricts Zika virus and tick-borne encephalitis virus replication by targeting NS3 for proteasomal degradation. *Journal of virology*, *92*(7), e02054-17.
34. Wakerley, B. R., & Yuki, N. (2013). Infectious and noninfectious triggers in Guillain–Barré syndrome. *Expert review of clinical immunology*, *9*(7), 627–639.
35. Van Doorn, P. A., Ruts, L., & Jacobs, B. C. (2008). Clinical features, pathogenesis, and treatment of Guillain-Barré syndrome. *The Lancet Neurology*, *7*(10), 939-950.
36. Musso, D., Ko, A. I., & Baud, D. (2019). Zika Virus Infection — After the Pandemic. *New England Journal of Medicine*, *381*(15), 1444–1457. https://doi.org/10.1056/NEJMRA1808246
37. *Guillain-Barré Syndrome | National Institute of Neurological Disorders and Stroke*. (n.d.). Retrieved March 31, 2023, from https://www.ninds.nih.gov/health-information/disorders/guillain-barre-syndrome

