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IN SILICO STUDIES ON DENGUE AND ZIKA VIRAL PROTEINS WITH SELECTED EMBLICA OFFICINALIS GAERTN CONSTITUENTS

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ABSTRACT

Medicinal plants are the precious gift of nature which plays vital role in health care sector for developing nation and potent source of therapeutic molecules to heal various diseases in the world. *Emblica officinalis Gaertn* (Amla) is widely used in the Indian system of medicine and believed to increase defense against diseases and is also known for its therapeutic properties. Phytochemicals present in *Emblica officinalis Gaertn* are found to have anti-inflammatory, antibacterial and antioxidant properties. This article describes the study of the binding efficiency of the selected 4 compounds that are present in the *Emblica officinalis* with seven proteins from Dengue virus and six proteins from Zika virus through in silico methods. By our virtual screening and docking result, we found that the Benzoic acid,3,4,5-trihydoxy- Compound has highest binding affinity with the proteins of Dengue and Zika virus.

KEYWORDS: Amla, Dengue virus, Zika virus, hydrogen bond, binding affinities.

1. INTRODUCTION

Medicinal plants had played an important role in the development of human culture. Medicinal plants are resources of traditional medicines and many of the modern medicines are produced indirectly from plants.[1] Amla which is known as Emblica officinalis is an Indian herb which is extensively used in ayurvedic system of medicine. *Emblica officinalis Gaertn* (*Phyllanthus emblica Linn.* Amla, Indian Gooseberry) known for its therapeutic properties belongs to the *Euphorbiacea* family.[2] *Emblica officinalis* is a tree indigenous to tropical regions of Southeast Asia. The tree produces a fruit commonly known as Indian Gooseberry or Amla. The root, bark and leaves of this tree are used for the treatment of certain problems like indigestion, diarrhea, dysentery, eczema and warts.[3] The fruits of this tree act as antioxidants, immunomodulatory agents and cytoprotective against chromium. Amla is highly nutritious and is an important dietary source of vitamin C, minerals, and amino acids.[4] It contains several chemical constituents like tannins, alkaloids and phenols and among all hydrolysable tannins, Emblicanin A and B; gallic acid, ellagic acid are reported to possess biological activity.[5] Extracts from these fruits has been used in traditional medicine for generations to treat symptoms ranging from constipation to the treatment of tumors.[6] Amla or Indian gooseberry is used under many conditions like liver injury, atherosclerosis and diabetes and it also posseses a very good hypocholestremic effect.[7] Amla is also found to enhance interferon production. Amla powder and oil are used traditionally in Ayurvedic applications for the treatment of scalp. Amla powder improves immunity and gives physical strength.[8] It improves complexion and removes wrinkles. Amla is also used to treat constipation and is used as a cooling agent to reduce the effects of sun strokes and sun burns.

The fruit contains high amounts of ascorbic acid or Vitamin C and high density of ellagitannins such as emblicanin A (37%), emblicanin B (33%), punigluconin (12%) and pedunculagin (14%). It also contains punicafolin and phyllanemblinin A, phyllanemblin other polyphenols: flavonoids, kaempferol, ellagic acid and gallic acid.[9] GC-MS chromatogram of the leaves of methanolic extract of *Emblica officinalis* showed four major peaks and has been identified after comparison of the mass spectra with NIST library, indicating the presence of four phytocomponents and its medicinal properties. From the results, it was observed that presence of 1, 2, 3-benzenetriol (synonym: Pyrogallol), 2- Furancarboxaldehyde, 5-(hydroxymethyl) - (synonym: 5- hydroxymethylfurfural), 2-Acetyl-5-methylfuran (synonym: 5-methyl-2-furylmethylketone), Benzoic acid, 3, 4, 5- trihydroxy- (synonym: Gallic-acid) were the major components in the extract. Pyrogallol is a polyphenol is known for its fungicidal and fungi static properties. Pyrogallol is reported to be an effective

antimicrobial agent and its toxicity is attributed to the three hydroxyl groups present in its structure. In addition, pyrogallol has also shown antitumor, antiviral, antibacterial, cardioprotective, prooxidant and anti-mutagenic activities. The gallic acid and its derivatives were reported to have a wide spectrum of biological activities like antimicrobial, anticancer, antiviral, anti-inflammatory, analgesic and anti-HIV activities.[10]

Dengue, a haemorrhagic fever,[11] is caused due to all four serotypes of dengue virus (DENV-1, DENV-2, DENV-3 and DENV-4).[12] These viruses contain ten proteins out of which three are structural proteins and seven are non structural proteins.[13] The seven non structural proteins are capsid protein, envelope protein, NS1 protein, transmembrane domain of NS2A, NS2B/NS3 protease, NS3 helicase and NS5 protein. NS2B-NS3 protease is a crucial enzyme for the viral replication.[14] This protein is hetero dimeric protein of NS2B and NS3protein. The N-terminal of the NS3 protein forms associates with the NS2B cofactor which is important for the viral replication. NS2B/ NS3 protease has an important role in the viral life cycle.[15] Envelope protein is a structural protein which is involved in the viral assembly. The protein utilized for the study is the envelope protein domain III of the dengue type 4 viruses (strain Dominica / 814669 / 1981). It is classified under structural protein immune system.[16] The capsid protein is one of the structural proteins, which is involved in the encapsidation of the viral genome. The capsid protein used for this study was from dengue virus type 2 (strain Puerto Rico/PR159-S1/1969).[17] The protein used for this study was the trans-membrane domain of theNS2A of dengue virus type 2. NS2A is a non structural protein and it is a component of viral replication complex which is functionally active in the assembly of the virion and also it acts as an antagonist to the host immune response.[18] NS3 helicase belongs to the non-structural and a multi-domain dengue virus replication protein.[19] The protein used for this study is the non-structural 5 (NS5) protein from the dengue virus type 3 (strain Sri Lanka / 1266 / 2000). This protein is classified under the transferases. The RNA dependent RNA polymerase (RdRp) domain of the NS5 protein isinvolved in the replication of the viral genome. RNA is synthesized via "de novo" by NS5 protein.[20]

Zika virus (ZIKV) is an emerging mosquito-borne virus and member of the family Flaviviridae. ZIKV is transmitted by Aedes mosquitoes, with humans representing the amplifying host.[21] Zika virus (ZIKV) infection has been a source of concern in the recent few months due to increase in the number of patients being affected by it with epidemic proportions in Brazil and its potential of spread to other countries. The association of microcephaly in new-borns due to Zika virus has further created panic and worry among the people.[22] There was anticipation that a ZIKV outbreak in India was possible due to the ubiquitous presence of the vector, *Aedes aegypti* mosquitoes and the susceptible host.[23] Substantial evidence now indicates that Zika virus can be transmitted from the mother to the fetus during pregnancy.[24] ZIKV has a single-stranded positive-sense genome of approximately 11 Kb.[25] The viral RNA includes a complete open reading frame sequence, encoding for a polyprotein with three structural components (capsid [C], premembrane [prM] or membrane [M], and envelope [E]) and seven non-structural proteins (NS1, NS2a, NS2b, NS3, NS4a, NS4b, and NS5).[26] NS1 glycoprotein plays an anchoring role in fetal pathologies especially the microcephaly while NS2B and NS3 have protease function and process the polyprotein.[27] The nonstructural protein 5 of *Zika virus* (ZIKV-NS5) is critical for ZIKV replication through the 5'-RNA capping and RNA polymerase activities present in its N-terminal methyltransferase (MTase) and C-terminal RNA-dependent RNA polymerase (RdRp) domains, respectively.[28] ZIKV non-structural protein 4A (NS4A) impairs the RLR-mitochondrial antiviral-signaling protein (MAVS) interaction and subsequent induction of antiviral immune responses.[29] Zika virus infection during pregnancy can result a serious birth defect called microcephaly and also other serious foetal brain defects which became grave health issues recently.[30] The common features of ZIKV infection are fever, conjunctivitis, cutaneous rash, and arthralgia but the majority of the affected patients with the clinical disease present with only mild symptoms.[31] Recently, sofosbuvir an antiviral is clinically approved for treating Zika infection and Novobiocin previously an antibiotic is now used as a potent anti Zika drug.

Bioinformatics is an interdisciplinary branch of science which utilizes statistics, computer and mathematics to analyse biological data.[32] Bioinformatics is now utilized for many researches to identify many aspects such as evolution. Protein Data Bank (PDB) is a protein storage bioinformatics tool. It contains the structures of large numbers of proteins, ligands and other macromolecules.[33] Docking analysis can be conducted for the protein and the ligand to analyse the fitness and the interaction with each other in the form of energy. This interaction could be used as the pharmaceutical approach for drug production.[34]

The aim of our study is to compare the best docking fit for the selected *Emblica officinalis Gaertn* constituents with the Dengue and Zika viral proteins.

2. MATERIALS AND METHODOLOGIES

2.1. Preparation of Dengue and Zika viral proteins

The protein data bank (PDB) was used to obtain the three-dimensional structure of the macromolecule. PDB contains large number of proteins which are experimentally determined and stored in this site. The structures are downloaded and saved either in mm CIF or PDB format. Proteins of dengue and Zika virus which were identified and numbered in the protein data bank were used for this study. Two structural proteins and five

non-structural proteins of dengue virus and two structural and four non-structural proteins of Zika virus was downloaded from protein data bank and used for this study. The downloaded proteins were viewed in Py-Mol viewer.[35]

2.2. Preparation of ligands

Ligands selected were from the previous studies on GCMS analysis on *Emblica officinalis Gaertn* extract. 4 ligands were used for the study. Ligands were constructed using Chem Sketch.[36] Chemsketch is a software that can be used to produce structures of organic molecules, names of organic molecules as well as Lewis structures, 3D structures, space filling models or ball and stick models, among other things. The constructed ligands were optimized to add the hydrogen bonds and the obtained structures were saved in mol for docking analysis and named as A, B and C respectively.

2.3. Docking study

Docking studies were conducting using iGEMDOCK software. IGEMDOCK (Generic Evolutionary Method for molecular Docking) is a graphical-automatic drug design system for docking, screening and post-analysis.[37] iGEMDOCK provides the visualizations of the protein-compound interaction profiles and even the hierarchical clustering dendrogram of the compounds for post-screening analysis. The proteins and the ligands were loaded and the out path was set. Standard docking parameters were used for docking (population size=200, generations =70 and Number of solutions =2). The docking process was initiated. After the docking process, the best docking pose for the individual ligands can be obtained for all the seven dengue viral proteins. The best binding pose, the binding affinity and the total binding energy values were saved in the output folder. The saved files were visualized in Py-Mol viewer.[38]

3. RESULTS

3.1. Total Binding Energy (kcal/mol) profile for Dengue and Zika viruses non structural proteins with 4 ligands.

Table 1: The Total Binding Energy (kcal/mol) profile for Dengue and Zika viruses non structural proteins with 4 ligands.

Ligand	Compound name	Dengue Virus					Zika virus			
		NS1 protein	Trans membrane domain of NS2A	NS2B / NS3 protease	NS3 helicase	NS5 protein	NS1 protein	NS2B / NS3 protease	NS3 helicase	NS5 protein
A	1,2,3-Benzenetriol	-84.55	-52.81	-59.12	-73.39	-66.92	-67.83	-65.6	-69.13	-66.81
B	2-Furancarboxaldehyde,5-(hydroxymethyl)-	-69.19	-53.43	-63.69	-69.44	-61.36	-64.78	-76.86	-79.33	-69.53
C	2-Acetyl-5-methylfuran	-65.06	-52.34	-56.4	-62.21	-61.55	-64.41	-69.8	-71.1	-62.08
D	Benzoic acid,3,4,5-trihydoxy-	-88.73	-66.8	-64.56	-87.96	-77.16	-86.31	-75.29	-100.45	-81.76

3.2. Total Binding Energy (kcal/mol) profile for Dengue and Zika viruses structural proteins with 4 ligands.

Table 2: The Total Binding Energy (kcal/mol) profile for Dengue and Zika viruses structural proteins with 4 ligands.

Ligand	Compound name	Dengue virus		Zika virus	
		Capsid protein	Envelope protein	Capsid protein	Envelope protein
A	1,2,3-Benzenetriol	-62.44	-70.17	-67.03	-57.68
B	2-Furancarboxaldehyde,5-(hydroxymethyl)-	-70.09	-64.8	-84.06	-61.43
C	2-Acetyl-5-methylfuran	-64.12	-60.85	-65.81	-57.92
D	Benzoic acid,3,4,5-trihydoxy-	-80.64	-83.79	-94.98	-65.07

3.3. H – Bond profile for Dengue and Zika viruses non structural protein with 4 ligands.

Table 3: H – Bond profile for Dengue and Zika viruses non structural proteins with 4 ligands.

Ligand	Compound name	Dengue virus					Zika virus			
		NS1 protein	Trans membrane domain of NS2A	NS2B / NS3 protease	NS3 helicase	NS5 protein	NS1 protein	NS2B / NS3 protease	NS3 helicase	NS5 protein
A	1,2,3-Benzenetriol	H-S H-M	H-S H-M	H-S H-M	H-S H-M	H-S H-M	H-M H-M	H-S H-M	H-S H-M	H-S H-M
B	2-Furancarboxaldehyde,5-(hydroxymethyl)-	H-S H-M	H-S H-M	H-S H-M	H-S	H-S H-M	H-S H-M	H-S H-M	H-S H-M	H-S H-M
C	2-Acetyl-5-methylfuran	H-S H-M	H-S H-M	H-S H-M	H-S	H-S H-M	H-M	H-M	H-S H-M	H-M
D	Benzoic acid,3,4,5-trihydoxy-	H-S H-M	H-S H-M	H-S H-M	H-S H-M	H-S H-M	H-S H-M	H-M	H-S H-M	H-S

3.4. H - Bond profile for Dengue and Zika viruses structural protein with 4 ligands.

Table 4: H – bond profile for Dengue and Zika viruses structural proteins with 4 ligands.

Ligand	Compound name	Dengue virus		Zika virus	
		Capsid protein	Envelope protein	Capsid protein	Envelope protein
A	1,2,3-Benzenetriol	H-S H-M	H-M	H-M	H-S H-M
B	2-Furancarboxaldehyde,5-(hydroxymethyl)-	H-S H-M	H-S H-M	H-S H-M	H-S H-M
C	2-Acetyl-5-methylfuran	H-S H-M	H-M	H-M	H-M
D	Benzoic acid,3,4,5-trihydoxy-	H-S	H-S H-M	H-S H-M	H-S H-M

3.5. Amino acid position profile for Dengue and Zika viruses non structural protein with 4 ligands.

Table 5: Amino acid position profile for Dengue and Zika viruses non structural proteins with 4 ligands.

Ligand	Compound name	Dengue Virus					Zika virus			
		NS1 protein	Trans membrane domain of NS2A	NS2B / NS3 protease	NS3 helicase	NS5 protein	NS1 protein	NS2B / NS3 protease	NS3 helicase	NS5 protein
A	1,2,3-Benzenetriol	Asn (255)	Gly (3)	Asp (58)	Asn (329)	Gly (86)	Arg (314)	Thr(1134) Ala(1135)	Lys (200)	Gly (86)
B	2-Furancarboxaldehyde,5-(hydroxymethyl)-	Arg (294)	Ile(2) Gly(3) Thr(7)	Gly (87)	Arg (268)	Thr (51)	Glu (310)	Gly (1151)	Lys (200)	Cys (667)

C	2-Acetyl-5-methylfuran	Ile (242) Asn (255)	Gly (3)	Arg (55)	Asp(541)	Asp (808)	Glu (315) Cys (316)	Gly(1151)	Arg (459)	Asp (599)
D	Benzoic acid,3,4,5-trihydoxy-	Asn (255)	Gly (3)	Asn (152)	Asp(329)	Val (132)	Arg (314)	Val(1126) Gly(1151) Asn(1152) Gly(1153)	Lys (200) Arg (459)	Lys (462)

3.6. Amino acid position profile for Dengue and Zika viruses structural protein with 4 ligands

Table 6: Amino acid position profile for Dengue and Zika viruses structural proteins with 4 ligands.

Ligand	Compound name	Dengue virus		Zika virus	
		Capsid protein	Envelope protein	Capsid protein	Envelope protein
A	1,2,3-Benzenetriol	Leu(46) Arg(41)	Arg(629)	Leu(38)	Ala(272)
B	2-Furancarboxaldehyde,5-(hydroxymethyl)-	Thr(62)	Arg(672)	Arg(32)	Ala(227
C	2-Acetyl-5-methylfuran	Arg(41)	Arg(629)	Gly(36) Leu(37) Leu(38)	Thr(366)
D	Benzoic acid,3,4,5-trihydoxy-	Arg(41)	Lys(625)	Arg(32) Leu(38)	Arg(357)

4. DISCUSSION

Considering all the tables from Table – 1, to Table - 6, the 3D structure coordinates of seven non proteins of dengue and six proteins of Zika virus are optimized and 4 compounds from *Emblica officinalis* extract are identified. The total binding energy of the compounds with all the thirteen proteins was calculated using iGEMDOCK. Evaluations of binding conformation of these 4 compounds with seven dengue as well as six Zika viral proteins are performed using iGEMDOCK. From docking study, we listed binding affinities of 4 compounds based on ligand binding energy (Table- 1 and Table - 2). The binding pose for each ligand molecule into the dengue and Zika viral proteins are analyzed and the one having lowest ligand binding energy with these proteins among the different poses are generated. The lower energy scores represent better protein-ligand target binding affinity compared to higher energy score. Considering the structural proteins of Dengue virus, among the 4 analogs, compound "D" is found to have lower ligand binding energy (binding energy value= -83.79 kcal/mol), than other analogs for Envelope protein. Compound "D" has least binding energy score with caspid protein (binding energy value= -80.64 kcal/mol), the structural proteins of Zika virus have following binding energies, Envelope protein('D' binding energy value= -65.07 kcal/mol) and Capsid protein('D' binding energy value= -94.98 kcal/mol). The non structural proteins of Dengue virus had these binding energy values: NS1 protein ('D', binding energy value = -88.73 kcal/mol), Trans membrane domain of NS2A ('D', binding energy value= -66.8 kcal/mol), NS2B / NS3 protease ('D', binding energy value= -64.56 kcal/mol), NS3 helicase ('D', binding energy value= -87.96 kcal/mol) and NS5 protein ('D', binding energy value= -77.16 kcal/mol). The non structural proteins of Zika virus have the following binding energy values: NS1 protein ('D', binding energy value= -86.31 kcal/mol), NS2B / NS3 protease ('B', binding energy value= -76.86 kcal/mol) NS3 helicase ('D', binding energy values= -100.45 kcal/mol) and NS5 protein ('D', binding energy values= -81.76 kcal/mol). We further analyzed the docked pose for finding the binding mode of compound "D" for seven dengue and six zika viral proteins to validate the reasonable binding conformations.

4.1. Non-Structural proteins of Dengue Virus

4.1.1. The Total Binding Energy for Dengue virus NS1 protein with 4 ligands

From Table – 1, Table – 3 and Table – 5, the docking simulation of 4 ligands were performed for Dengue virus NS1 protein. From the docking study, we observed that compound – D has best binding affinity with the target NS1 protein with the binding energy value of -88.73 kcal/mol. Interaction analysis of binding mode of compound –D in dengue virus NS1 protein reveals that it forms two hydrogen bonds of low energy with Asn (255) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus NS1 protein with 4 ligands is shown in Fig.1.

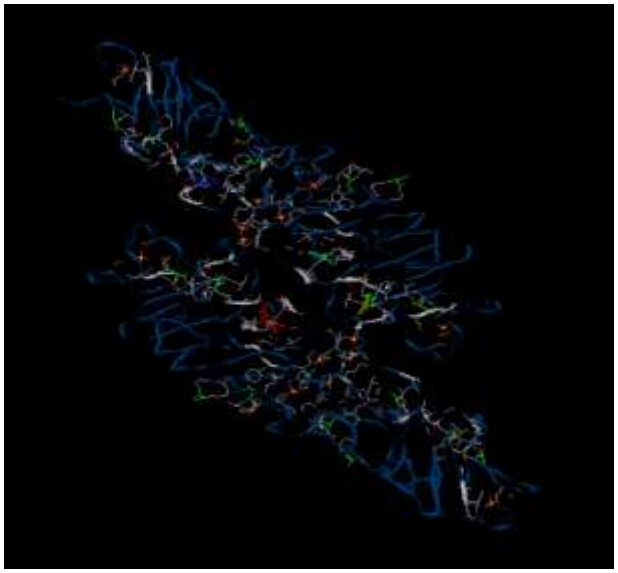

Fig. 1: The Total Binding Energy profile for Dengue virus NS1 protein with 4 ligands.

4.1.2. The Total Binding Energy for Dengue virus Trans membrane domain of NS2A with 4 ligands

From Table – 1, Table – 3 and Table – 5, the docking simulation of 4 ligands were performed for Dengue virus Trans membrane domain of NS2A. From the docking study, we observed that compound – D has best binding affinity with the target Trans membrane domain of NS2A with the binding energy value of -66.8 kcal/mol. Interaction analysis of binding mode of compound –D in dengue virus Trans membrane domain of NS2A protein reveals that it forms two hydrogen bonds of low energy with Gly(3) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus Trans membrane domain of NS2A with 4 ligands is shown in Fig.2.

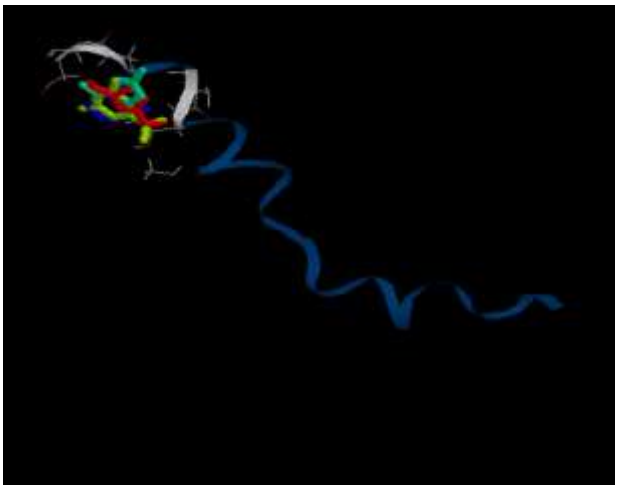

Fig. 2: The Total Binding Energy profile for Dengue virus Trans membrane domain of NS2A with 4 ligands.

4.1.3. The Total Binding Energy for Dengue virus NS2B / NS3 protease with 4 ligands

From Table – 1, Table – 3 and Table – 5, the docking simulation of 4 ligands were performed for Dengue virus NS2B / NS3 protease. From the docking study, we observed that compound – D has best binding affinity with the target NS2B / NS3 protease with the binding energy value of -64.56 kcal/mol. Interaction analysis of binding mode of compound – D in dengue virus NS2B/ NS3 protease reveals that it forms two hydrogen bonds of low energy with Asn(152) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus NS2B / NS3 protease with 4 ligands is shown in Fig.3.

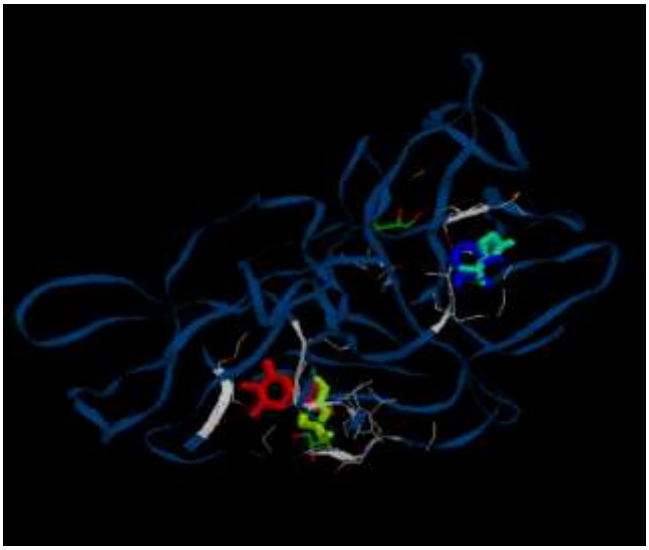

Fig. 3: The Total Binding Energy profile for Dengue virus NS2B / NS3 protease with 3 ligands.

4.1.4. The Total Binding Energy for Dengue virus NS3 helicase with 4 ligands

From Table – 1, Table – 3 and Table – 5, the docking simulation of 4 ligands were performed for Dengue virus NS3 helicase. From the docking study, we observed that compound – D has best binding affinity with the target NS3 helicase with the binding energy value of -87.96 kcal/mol. Interaction analysis of binding mode of compound –D in dengue virus NS3 helicase reveals that it forms two hydrogen bonds of low energy with Asp(329) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus NS3 helicase with 4 ligands is shown in Fig.4.

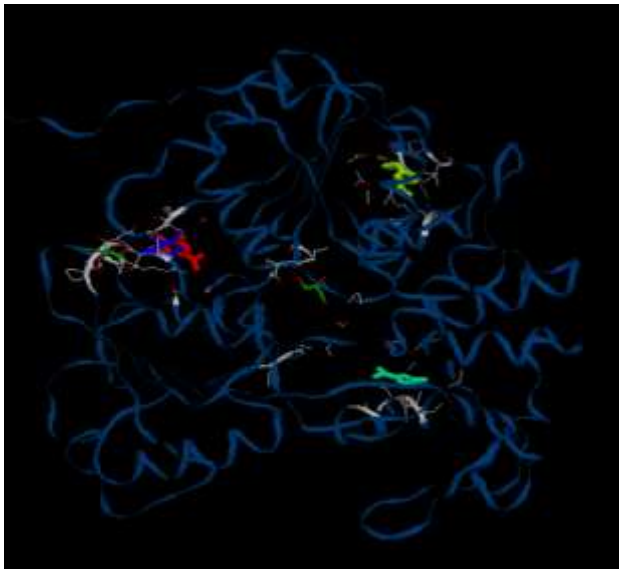

Fig. 4: The Total Binding Energy profile for Dengue virus NS3 helicase with 4 ligands.

4.1.5. The Total Binding Energy for Dengue virus NS5 protein with 4 ligands

From Table – 1, Table – 3 and Table – 5, the docking simulation of 4 ligands were performed for Dengue virus NS5 protein From the docking study, we observed that compound – D has best binding affinity with the target NS5 protein with the binding energy value of -77.16 kcal/mol. Interaction analysis of binding mode of compound –D in dengue virus NS5 protein reveals that it forms two hydrogen bonds of low energy with Val (132) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus NS5 protein with 4 ligands is shown in Fig.5.

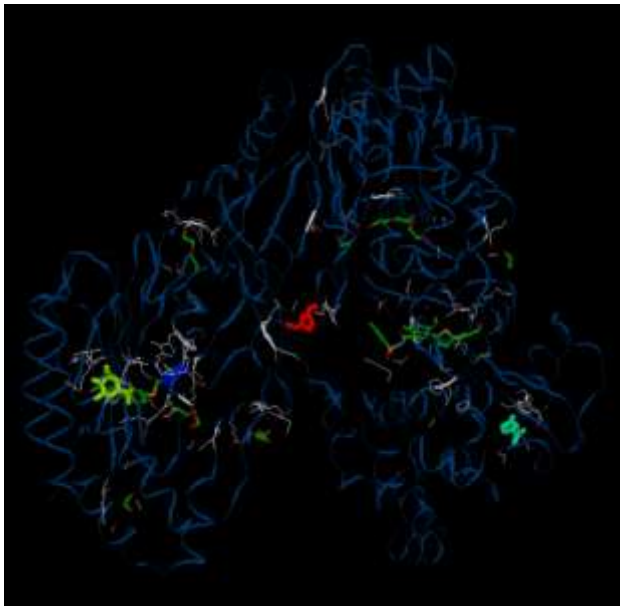

Fig. 5: The Total Binding Energy profile for Dengue virus NS5 protein with 4 ligands

4.2. Non-Structural proteins of Zika Virus

4.2.1. The Total Binding Energy for Zika virus NS1 protein with 4 ligands

From Table – 1, Table – 3 and Table – 5, the docking simulation of 4 ligands were performed for Zika virus NS1 protein. From the docking study, we observed that compound –D has best binding affinity with the target NS1 protein with the binding energy values of -86.31 kcal/mol. Interaction analysis of binding mode of compounds –D in Zika virus NS1 protein reveals that it forms two hydrogen bonds of low energy with Arg(314) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Zika virus NS1 protein with 4 ligands is shown in Fig.6.

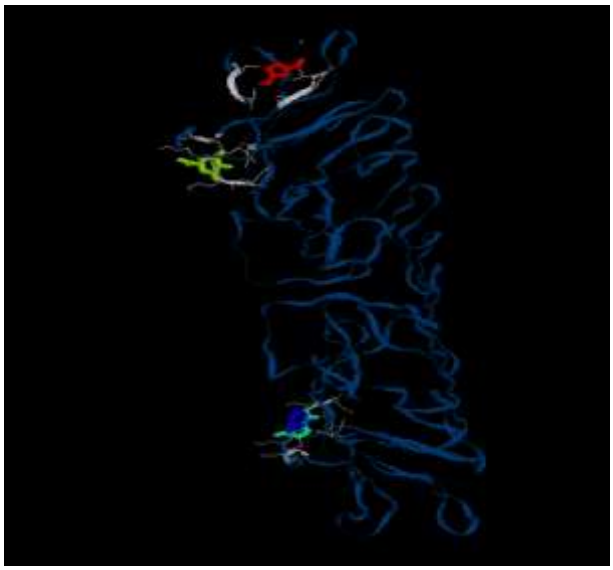

Fig. 6: The Total Binding Energy profile for Zika virus NS1 protein with 4 ligands

4.2.2. The Total Binding Energy for Zika virus NS2B / NS3 protease with 4 ligands

From Table – 1, Table – 3 and Table – 5, the docking simulation of 4 ligands were performed for Zika virus NS2B / NS3 protease. From the docking study, we observed that compound – B has best binding affinity with the target NS2B / NS3 protease with the binding energy value of -76.86 kcal/mol. Interaction analysis of binding mode of compound –B in Zika virus NS2B / NS3 protease reveals that it forms two hydrogen bonds of low energy with Gly(1151) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Zika virus NS2B / NS3 protease with 4 ligands is shown in Fig.7.

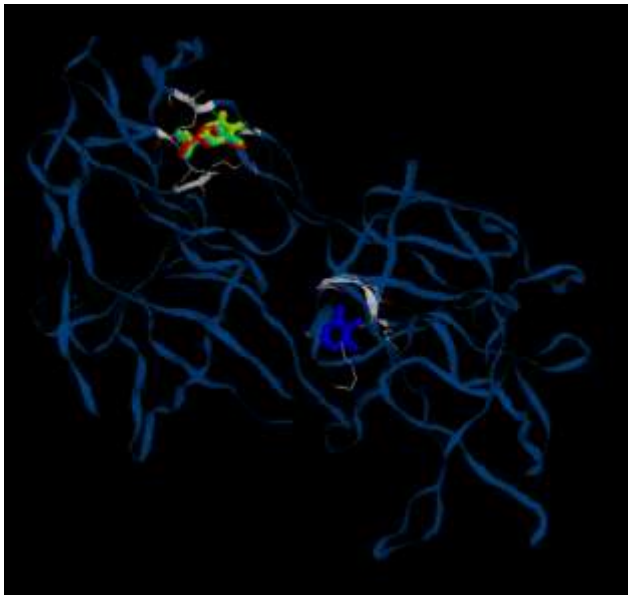

Fig. 7: The Total Binding Energy profile for Zika virus NS2B / NS3 protease with 4 ligands.

4.2.3. The Total Binding Energy for Zika virus with NS3 helicase with 4 ligands

From Table – 1, Table – 3 and Table – 5, the docking simulation of 4 ligands were performed for Zika virus NS3 helicase. From the docking study, we observed that compound –D has best binding affinity with the target NS3 helicase with the binding energy value of -100.45 kcal/mol. Interaction analysis of binding mode of compound –D in Zika virus NS3 helicase reveals that it forms two hydrogen bonds of low energy with Lys (200) and Arg(459) residues.A close-up view of the Total Binding Energy (kcal/mol) profile for Zika virus NS3 helicase with 4 ligands is shown in Fig.8.

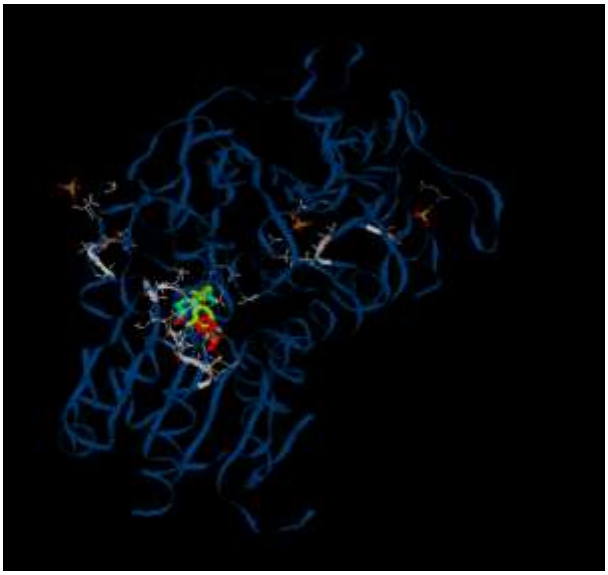

Fig. 8: The Total Binding Energy profile for Zika virus NS3 helicase with 4 ligands.

4.2.4. The Total Binding Energy for Zika virus with NS5 protein protein with 4 ligands

From Table – 1, Table – 3 and Table – 5, the docking simulation of 4 ligands were performed for Zika virus NS5 protein. From the docking study, we observed that compound –D has best binding affinity with the target NS5 protein with the binding energy value of -81.76 kcal/mol. Interaction analysis of binding mode of compound –D in Zika virus NS5 protein reveals that it forms one hydrogen bond of low energy with Lys(462) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Zika virus NS5 protein with 4 ligands is shown in Fig.9.

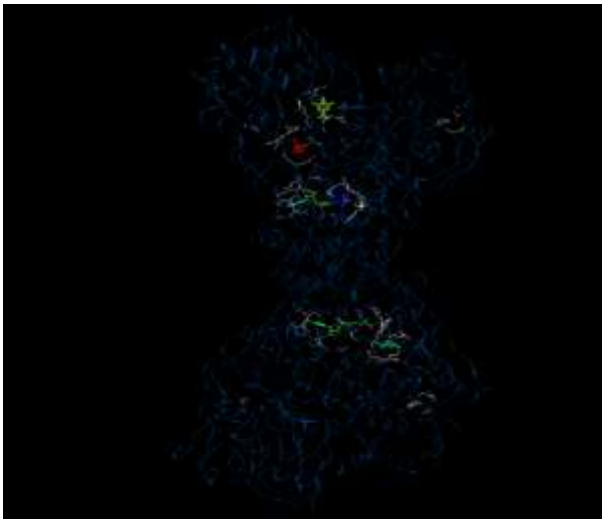

Fig. 9: The Total Binding Energy profile for Zika virus NS5 proteins with 4 ligands.

4.3. Structural proteins of Dengue virus

4.3.1. The Total Binding Energy for Dengue virus Capsid protein with 4 ligands

From Table – 2, Table – 4 and Table – 6, the docking simulation of 4 ligands were performed for Dengue virus Capsid protein. From the docking study, we observed that compound – D has best binding affinity with the target Capsid protein with the binding energy value of -80.64 kcal/mol. Interaction analysis of binding mode of compound –D in dengue virus Capsid protein reveals that it forms one hydrogen bond of low energy with Arg(41) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus Capsid protein with 4 ligands is shown in Fig.10.

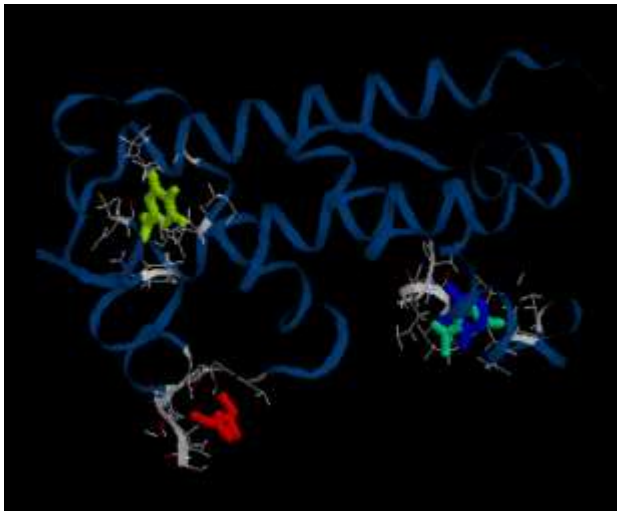

Fig. 10: The Total Binding Energy profile for Dengue virus Capsid protein with 4 ligands.

4.3.2. The Total Binding Energy for Dengue virus envelope protein with 4 ligands

From Table – 2, Table – 4 and Table – 6, the docking simulation of 4 ligands were performed for Dengue virus envelope protein. From the docking study, we observed that compound –D has best binding affinity with the target envelope protein with the binding energy value of -83.79 kcal/mol. Interaction analysis of binding mode of compound –D in dengue virus envelope protein reveals that it forms two hydrogen bonds of low energy with Lys(625) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus envelope protein with 4 ligands is shown in Fig.11.

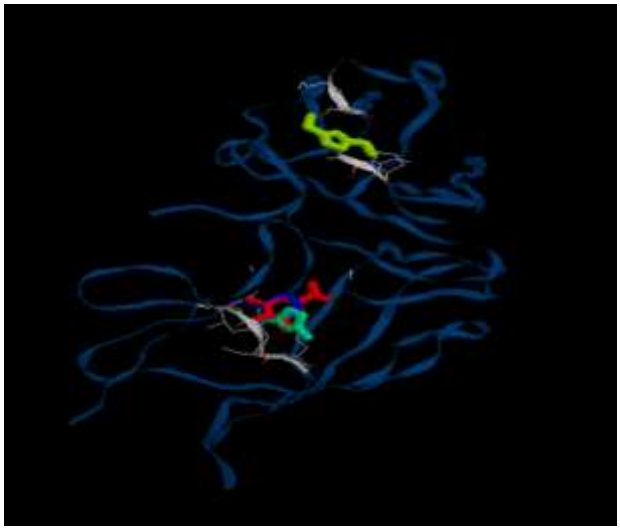

Fig. 11: The Total Binding Energy profile for Dengue virus envelope protein with 4 ligands.

4.4. Structural proteins of Zika virus

4.4.1. The Total Binding Energy for Zika virus Capsid protein with 4 ligands

From Table – 2, Table – 4 and Table – 6, the docking simulation of 4 ligands were performed for Zika virus Capsid protein. From the docking study, we observed that compound –D has best binding affinity with the target Capsid protein with the binding energy value of -94.98 kcal/mol. Interaction analysis of binding mode of compound –D in Zika virus capsid protein reveals that it forms two hydrogen bonds of low energy with Arg(32) and Leu(38) residues. A close-up view of the Total Binding Energy (kcal/mol) profile for Zika virus Capsid with 4 ligands is shown in Fig.12.

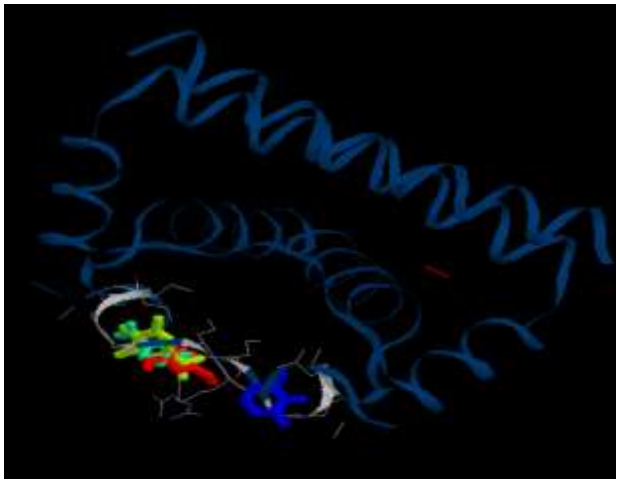

Fig. 12: The Total Binding Energy profile for Zika virus capsid protein with 4 ligands.

4.4.2. The Total Binding Energy for Zika virus Envelope protein with 4 ligands

From Table – 2, Table – 4 and Table – 6, the docking simulation of 4 ligands were performed for Zika virus Envelope protein. From the docking study, we observed that compound – D has best binding affinity with the target envelope protein with the binding energy value of -65.07 kcal/mol. Interaction analysis of binding mode of compound –D in Zika virus envelope protein reveals that it forms two hydrogen bonds of low energy with Arg(357) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Zika virus envelope protein with 4 ligands is shown in Fig.13.

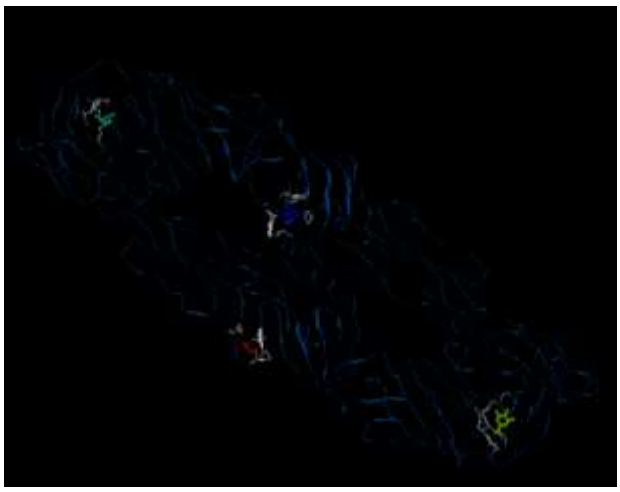

Fig. 13: The Total Binding Energy profile for Zika virus Envelope protein with 4 ligands.

5. CONCLUSION

Our molecular docking studies explored the possible binding modes of 4 compounds that are present in *Emblica officinalis* with seven proteins of Dengue virus and six proteins of Zika virus. Dengue virus consists of envelope protein, NS1 protein, Transmembrane doamin of NS2A, NS2B/NS3 protease, NS3 helicase, NS5 protein and capsid protein and Zika virus consists of NS1, NS2B/NS3 protease, NS3 helicase, NS5 protein It revealed that all the 4 compounds show minimum affinity with all the proteins. The compound D (Benzoic acid, 3, 4, 5-trihydoxy-) shows best results compared to other compounds. On comparing the binding energy and the binding site residues, we found that all the compounds differ in either of them for hydrogen bond formation. The conclusion which is drawn from our virtual screening and docking result are that the Compound D has highest binding affinity with all of the proteins of Dengue virus as well as most of the proteins of Zika virus except that compound B(2-Furancarboxaldehyde,5-(hydroxymethyl)- showed high binding affinity with NS2B/NS3 protease of Zika virus. Since the compound D is shown to have highest binding affinity with all of the non structural proteins of Dengue virus and most of the non structural proteins of Zika virus therefore it can be used as an effective drug target for Dengue virus as well as Zika virus. Hence, the Compound D may be considered as the effective drug target for both dengue and zika virus because it can effectively bind to most of the proteins of both the viruses. Though, there are many reports on the *in vitro* analysis of these compounds and its medicinal and toxic properties, there are no in silico studies that predict the binding and active regions especially with these proteins. Our study is an attempt to predict the binding site and the binding residues. However, validation of our results through *invivo* and *invitro* experiments and also with animal models will enlighten hope for the future development of more potent drugs for the treating Dengue and Zika.

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