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IN SILICO STUDIES ON DENGUE AND EBOLA VIRAL PROTEINS WITH SELECTED *OCIMUM SANCTUM* LEAVES CONSTITUENTS

[1]Anushree S., [1]Archana S., [1]Smriti Chawla, [1]Bhavya M., [1]Ramya M. and *[2]Balasubramanian Sathyamurthy

[1]Department of Biochemistry, Ramaiah College of Arts, Science and Commerce, Bangalore – 560054.

[*2]Professor, Department of Biochemistry, Ramaiah College of Arts, Science and Commerce, Bangalore – 560054.

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***Corresponding Author**
Dr. Balasubramanian Sathyamurthy
Professor, Department of Biochemistry, Ramaiah College of Arts, Science and Commerce, Bangalore – 560054.

ABSTRACT

Dengue and Ebola virus contains seven proteins, which are considered to be the most effective for drug designing. Recent studies have shown that these proteins can effectively cause the inactivation of dengue and ebola disease in humans. Phytochemicals present in *Ocimum sanctum* are found to have anti-inflamatory and antifungal properties. In this particular study, the binding efficiency of 3 compounds that is present in the *Ocimum sanctum* with all the fourteen proteins was performed through Insilico methods. By our virtual screening and molecular docking result, we found that the Benzene, 1, 2-dimethoxy-4-(1-propenyl) and Eugenol have highest binding affinity with the proteins and we also predicted the binding site amino acid residues and the type of hydrogen bonding.

KEYWORDS: Tulsi, molecular docking, hydrogen bonding, 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] It is an important element of indigenous medical systems in all over the world. The ethno botany provides a rich resource for research and development of natural drug.[2] Among all the plants *Ocimum sanctum*, also called as tulsi plays a great role for their therapeutic uses. Tulsi in the language of ayurveda is called as

"The Incomparable One," "Mother Medicine of Nature" and "The Queen of Herbs," and is known as an "elixir of life" that is without equal for both its medicinal and spiritual properties.[3] Ocimum belonging to family *Lamiaceae* are very important for their therapeutic potentials. *Ocimum sanctum* has two varieties i.e. black (Krishna Tulsi) and green (Rama Tulsi), their chemical constituents are similar.[4] *Ocimum sanctum* plants are considered as one of the most important source of medicine and drugs with many secondary metabolites and essential oils recommended for treatment of malaria, diarrhea, bronchial asthma, dysentery, bronchitis, skin diseases, arthritis, painful eye disease, chronic fever and eye diseases etc.[5,6] Apart from that *Ocimum sanctum* also shows some anticancerous, antifungal, antimicrobial, antifertility, hepatoprotective, antispasmodic, cardio protective, antiemetic, antidiabitic, analgesic, adaptogenic, and diaphoretic properties.[6,7,8,9]

GC-MS chromatogram of the methanolic extract of Ocimum sanctum showed three major peaks, Benzene, 1, 2-dimethoxy- 4- (2- propenyl) - (synonym: Methyl Isoeugenol), Isocaryophyllene (synonym: Caryophyllene) and Eugenol (Synonym: 2-Methoxy4-(2-propenyl) phenol) were the major components in the extract. Methyl-Isoeugenol has the property of Antifungal activity, Nematicidal activity and Antifeedant activity. Caryophyllene is widely known for its anti-inflammatory, cytotoxicity and antifungal activities. Eugenol is reported to possess Antimycotic Antiviral, Desinsection, Antiparasitic.[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]

Ebola virus is an aggressive pathogen that causes a highly lethal hemorrhagic fever syndrome in humans and nonhuman primates. *Ebola virus* and the related *Marburg virus* are members of the *Filovirus* family, that are pleomorphic, contain negative-sense RNA viruses whose genome organization is almost similar to the *Paramyxoviridae*. There are four strains of Ebola virus, among which the three—the Zaire, Ivory Coast, and Sudan strains—has shown to cause disease in both humans and nonhuman primates, with the Zaire strain exhibiting the highest lethality rate.[21] The genome of the Ebola virus is 19 kb long, which has seven open reading frames encoding structural proteins, including the virion envelope glycoprotein (GP), nucleoprotein (NP), and matrix proteins VP24 and VP40; non structural proteins, including VP30 and VP35; and the viral polymerase.[22] VP24 protein has effective role in inhibiting the host IFN response,[23] VP35 is a suppressor of RNA silencing and important for viral invasion of the innate immune response [24] VP30 has the primary role of initiating EBOV transcription.[25] VP40 protein has roles predominantly in viruses assembly and budding.[26,27] Glycoprotein has a critical role in attachment and fusion.[28,29,30] Both nucleoprotein and polymerase L protein has a distinct function in replication.[31]

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 *Ocimum sanctum* leaves constituents with the Dengue and Ebola viral proteins.

2. MATERIALS AND METHODOLOGIES

2.1. Preparation of Dengue and Ebola 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 ebola virus were used for this study. The 3D structure of all the fourteen proteins were downloaded from PDB and saved in PDB format. 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 *Ocimum sanctum* leaves extract.[10] 3 ligands were used for the study. Ligands were constructed using Chem Sketch.[36] 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] 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 Ebola viruses proteins with 3 ligands.

Table 1: The Total Binding Energy (kcal/mol) profile for Dengue and Ebola viruses non structural proteins with 3 ligands.

Ligand	Compound name	Dengue Virus					Ebola virus		
		NS1 protein	Trans membrane domain of NS2A	NS2B / NS3 protease	NS3 helicase	NS5 protein	VP30	Polymerase L-protein	VP35-RNA binding protein
A	Benzene,1,2-dimethoxy-4-(1-propenyl)	-85.9	-499.8	-70.2	-68.1	-67.6	-64.6	-73.8	-63.2
B	Caryophyllene	-84.2	-468.4	-66.2	-76	-67.1	-61.5	-65.6	-58.3
C	Eugenol	-80.1	-469.7	-70.9	-78.1	-77.6	-64.6	-63.1	-66.7

Table 2: The Total Binding Energy (kcal/mol) profile for Dengue and Ebola viruses structural proteins with 3 ligands.

Ligand	Compound name	Dengue virus		Ebola virus			
		Capsid protein	Envelope protein	Nucleoprotein	VP40- Matrix protein	VP24- Nucleocaspid protein	Glycoprotein
A	Benzene,1,2-dimethoxy-4-(1-propenyl)	-78.1	-71.1	-65.5	-67.7	-67.2	-84.7
B	Caryophyllene	-66	-56.5	-58.9	-62.4	-57.6	-75.2
C	Eugenol	-72.2	-70.1	-70.4	-70.1	-62.6	-91.7

3.2. H – Bond profile for Dengue and Ebola viruses protein with 3 ligands.

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

Ligand	Compound name	Dengue virus					Ebola virus		
		NS1 protein	Trans membrane domain of NS2A	NS2B / NS3 protease	NS3 helicase	NS5 protein	VP30	Polymerase L-protein	VP35-RNA binding protein
A	Benzene,1,2-dimethoxy -4-(1-propenyl)	H-M	-	H-S	-	H-S	H-S	H-M	-
B	Caryophyllene	-	-	-	-	-	-	-	-
C	Eugenol	H-M H-S	H-M	H-M	H-M H-S	H-M H-S	H-M	H-S	H-M

Table 4: H – bond profile for Dengue and Ebola viruses structural proteins with 3 ligands.

Ligand	Compound name	Dengue virus		Ebola virus			
		Capsid protein	Envelope protein	Nucleoprotein	VP40- Matrix protein	VP24- Nucleocaspid protein	Glycoprotein
A	Benzene,1,2-dimethoxy-4-(1-propenyl)	H-S	H-S	H-S	H-S	H-M	H-S
B	Caryophyllene	-	-	-	-	-	-
C	Eugenol	H-M H-S	H-M	H-M	H-M H-S	H-S	H-M

3.3. Amino acid position profile for Dengue and Ebola viruses protein with 3 ligands

Table 5: Amino acid position profile for Dengue and Ebola viruses non structural proteins with 3 ligands.

Ligand	Compound name	Dengue Virus					Ebola virus		
		NS1 protein	Trans membrane domain of NS2A	NS2B / NS3 protease	NS3 helicase	NS5 protein	VP30	Polymerase L-protein	VP35-RNA binding protein
A	Benzene,1,2-dimethoxy-4-(1-propenyl)	Ile(242)	-	Asn(152)	Pro(195) Asn (329)	Asn(69)	Arg(213)/ Gln(229)	Leu(368)	-
B	Caryophyllene	-	-	-	-	-	-	-	-
C	Eugenol	Ile(242) Asn(255)	Ala (14)	Glu(86)	-	Pro(298) Asp(359)	Thr(178)	Thr(206)	Asp(257)

Table 6: Amino acid position profile for Dengue and Ebola viruses structural proteins with 3 ligands.

Ligand	Compound name	Dengue virus		Ebola virus			
		Capsid protein	Envelope protein	Nucleoprotein	VP40- Matrix protein	VP24- Nucleocaspid protein	Glycoprotein
A	Benzene,1,2-dimethoxy -4-(1-propenyl)	Arg(41)	Arg(672)	His(737)	Arg(137)	Gln(83)	Trp(103)
B	Caryophyllene	-	-	-	-	-	-
C	Eugenol	Arg(41) Leu(44)	Arg(629)	His(737)	Ala(62) Arg(137)	Arg(137)	Trp(103)

4. DISCUSSION

Considering all the tables from Table – 1, to Table - 6, the 3D structure coordinates of seven non proteins of dengue and seven proteins of Ebola viruses are optimized and 3 compounds from *Ocimum sanctum* leaves extract are identified. The total binding energy of the compounds with all the fourteen proteins was calculated using iGEMDOCK. Evaluations of binding conformation of these 3 compounds with seven dengue as well as Ebola viral proteins are performed using iGEMDOCK. From docking study, we listed binding affinities of 3 compounds based on ligand binding energy (Table- 1 and Table - 2). The binding pose for each ligand molecule into the dengue and ebola 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 3 analogs, compound "A" is found to have lower ligand binding energy (binding energy value= -71.1 kcal/mol), than other analogs for Envelope protein. Compound "A" has least binding energy score with caspid protein (binding energy value= -78.1 kcal/mol), the structural proteins of ebola virus had following binding energies, Nucleoprotein('C' binding energy value= -70.4), VP40 Matrix protein('C' binding energy value= -70.1), VP24('A', binding energy value= -67.2), Glycoprotein('C', binding energy value= -91.7) The non structural proteins of Dengue virus had these binding energy values: Trans membrane domain of NS2A ('A', binding energy value= -499.8kcal/mol), NS2B / NS3 protease ('C', binding energy value= -70.9kcal/mol), NS3 helicase ('C', binding energy value= -78.1kcal/mol), NS5 protein ('C', binding energy value= -77.6 kcal/mol) and NS1 protein ('A', binding energy value = -85.9kcal/mol). And the non structural proteins of Ebola viruses have, VP35 ('C', binding energy value= -66.7), VP30 ('A & C', binding energy value= -64.6) and Polymerase L protein ('A', binding energy values= -73.8) We further analyzed the docked pose for finding the binding mode of compound "A" and compound "C" in to seven dengue and seven ebola 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 3 ligands

From Table – 1, Table – 3 and Table – 5, the docking simulation of 3 ligands were performed for Dengue virus NS1 protein. From the docking study, we observed that compound – A has best binding affinity with the target NS1 protein with the binding energy value of -85.9 kcal/mol . Interaction analysis of binding mode of compound –A in dengue virus NS1 protein

reveals that it forms one hydrogen bond with low energy, with Ile (242) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus NS1 protein with 3 ligands: is shown in Fig.1.

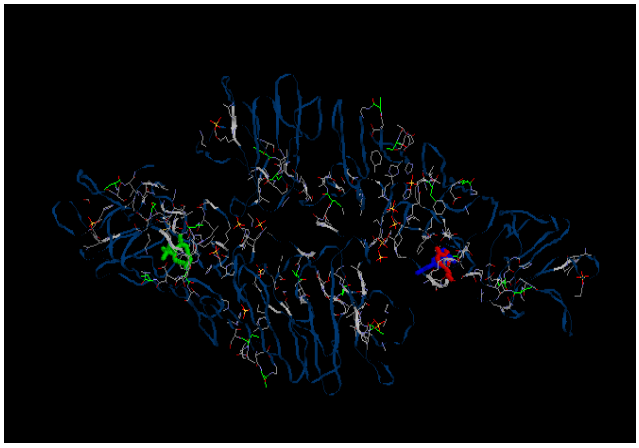

Fig. 1: The Total Binding Energy (kcal/mol) profile for Dengue virus NS1 protein with 3 ligands.

4.1.2. The Total Binding Energy for Dengue virus Trans membrane domain of NS2A with 3 ligands

From Table – 1, Table – 3 and Table – 5, the docking simulation of 3 ligands were performed for Dengue virus Trans membrane domain of NS2A. From the docking study, we observed that compound – A has best binding affinity with the target Trans membrane domain of NS2A with the binding energy value of -499.8 kcal/mol. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus Trans membrane domain of NS2A with 3 ligands: is shown in Fig.2.

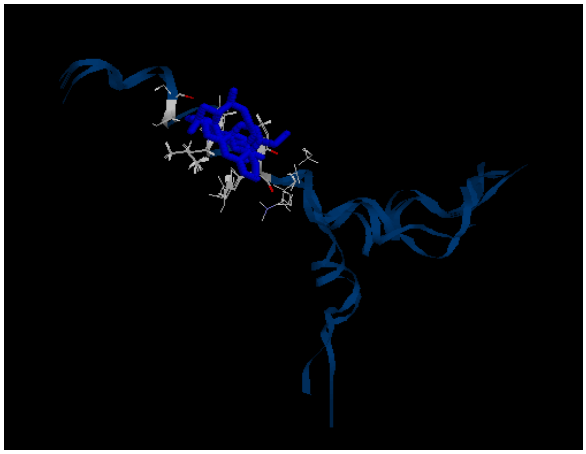

Fig. 2: The Total Binding Energy (kcal/mol) profile for Dengue virus Trans membrane domain of NS2A with 3 ligands.

4.1.3. The Total Binding Energy for Dengue virus NS2B / NS3 protease with 3 ligands

From Table – 1, Table – 3 and Table – 5, the docking simulation of 3 ligands were performed for Dengue virus NS2B / NS3 protease. From the docking study, we observed that compound – C has best binding affinity with the target NS2B / NS3 protease with the binding energy value of -70.9 kcal/mol. Interaction analysis of binding mode of compound –C in dengue virus NS2B / NS3 protease reveals that it forms one hydrogen bond with low energy, with Gly(87) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus NS2B / NS3 protease with 3 ligands: is shown in Fig.3.

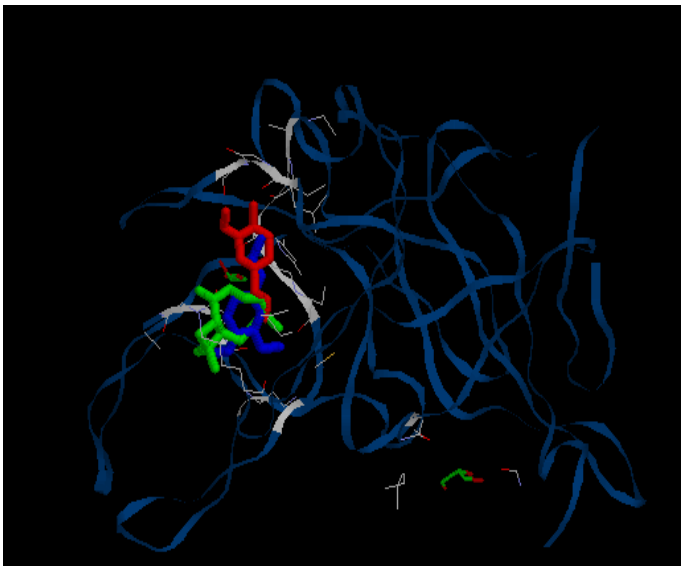

Fig. 3: The Total Binding Energy (kcal/mol) profile for Dengue virus NS2B / NS3 protease with 3 ligands.

4.1.4. The Total Binding Energy for Dengue virus NS3 helicase with 3 ligands

From Table – 1, Table – 3 and Table – 5, the docking simulation of 3 ligands were performed for Dengue virus NS3 helicase. From the docking study, we observed that compound – C has best binding affinity with the target NS3 helicase with the binding energy value of -78.1 kcal/mol. Interaction analysis of binding mode of compound –C in dengue virus NS3 helicase reveals that it forms two hydrogen bonds with low energy, with Asn (329) and Pro(195) residues. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus NS3 helicase with 3 ligands: is shown in Fig.4.

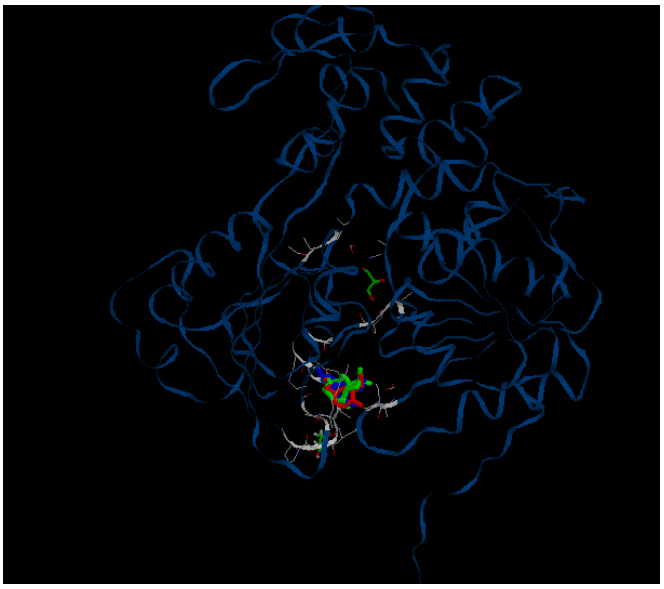

Fig. 4: The Total Binding Energy (kcal/mol) profile for Dengue virus NS3 helicase with 3 ligands.

4.1.5. The Total Binding Energy for Dengue virus NS5 protein with 3 ligands

From Table – 1, Table – 3 and Table – 5, the docking simulation of 3 ligands were performed for Dengue virus NS5 protein From the docking study, we observed that compound – C has best binding affinity with the target NS5 protein with the binding energy value of -77.6kcal/mol. Interaction analysis of binding mode of compound –C in dengue virus NS5 protein reveals that it forms two hydrogen bonds with low energy, with Pro (298) and Asp (359) residues. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus NS5 protein with 3 ligands: is shown in Fig.5.

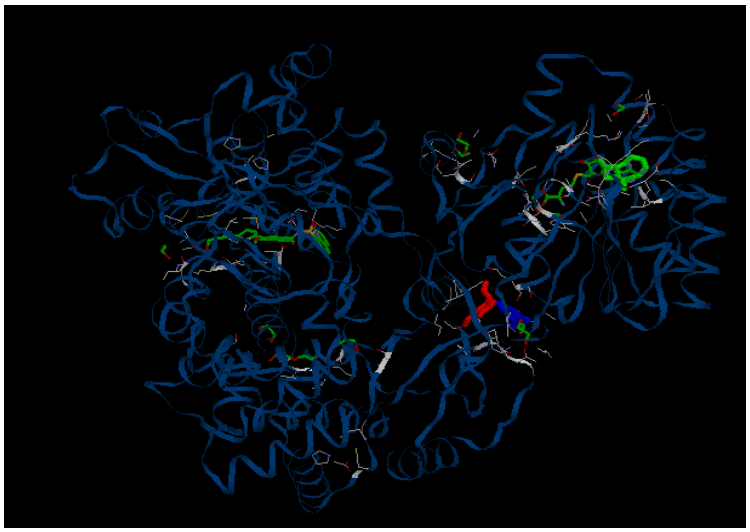

Fig. 5: The Total Binding Energy (kcal/mol) profile for Dengue virus NS5 protein with 3 ligands.

4.2. Non-Structural proteins of Ebola Virus

4.2.1. The Total Binding Energy for Ebola virus VP30 protein with 3 ligands

From Table – 1, Table – 3 and Table – 5, the docking simulation of 3 ligands were performed for Ebola virus VP30 protein. From the docking study, we observed that compounds – A and C has best binding affinity with the target VP30 protein with the binding energy values of -64.6 kcal/mol. Interaction analysis of binding mode of compounds –A and C in dengue virus VP30 protein reveals that it forms one hydrogen bond with low energy, with Arg (213), Gln (229) and Thr (178) residues. A close-up view of the Total Binding Energy (kcal/mol) profile for Ebola virus VP30 protein with 3 ligands: is shown in Fig.6.

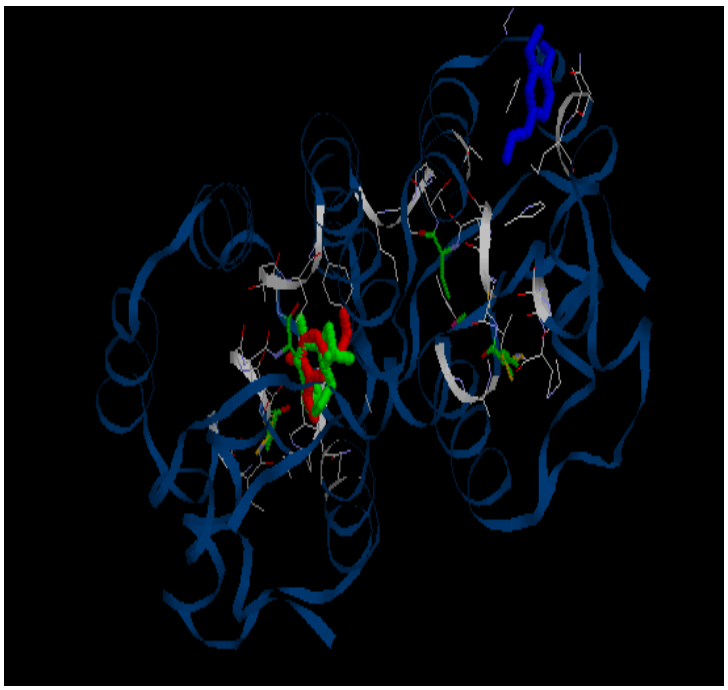

Fig. 6: The Total Binding Energy (kcal/mol) profile for Ebola virus VP30 protein with 3 ligands.

4.2.2. The Total Binding Energy for Ebola virus Polymerase L protein with 3 ligands

From Table – 1, Table – 3 and Table – 5, the docking simulation of 3 ligands were performed for Ebola virus Polymerase L protein From the docking study, we observed that compound – A has best binding affinity with the target Polymerase L protein with the binding energy value of -73.8kcal/mol. Interaction analysis of binding mode of compound –A in dengue virus Polymerase L protein reveals that it forms one hydrogen bond with low energy, with Leu (368) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Ebola virus Polymerase L protein with 3 ligands: is shown in Fig.7.

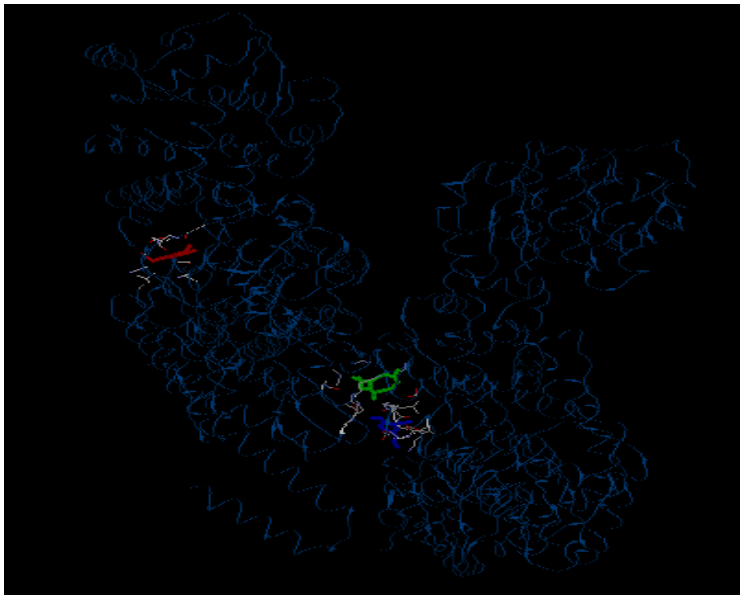

Fig. 7: The Total Binding Energy (kcal/mol) profile for Ebola virus Polymerase L protein with 3 ligands.

The Total Binding Energy for Ebola virus VP35 protein with 3 ligands

From Table – 1, Table – 3 and Table – 5, the docking simulation of 3 ligands were performed for Ebola virus VP35 protein. From the docking study, we observed that compound – C has best binding affinity with the target VP35 protein with the binding energy value of -66.7 kcal/mol. Interaction analysis of binding mode of compound –C in dengue virus VP35 protein reveals that it forms one hydrogen bond with low energy, with Asp(257) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Ebola virus VP35 protein with 3 ligands: is shown in Fig.8.

Fig. 8: The Total Binding Energy (kcal/mol) profile for Ebola virus VP35 protein with 3 ligands.

4.3. Structural proteins of Dengue virus

4.3.1. The Total Binding Energy for Dengue virus Capsid protein with 3 ligands

From Table – 2, Table – 4 and Table – 6, the docking simulation of 3 ligands were performed for Dengue virus Capsid protein. From the docking study, we observed that compound – A has best binding affinity with the target Capsid protein with the binding energy value of -78.1 kcal/mol. Interaction analysis of binding mode of compound –A in dengue virus Capsid protein reveals that it forms one hydrogen bond with low energy, with Arg(41) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus Capsid protein with 3 ligands: is shown in Fig.9.

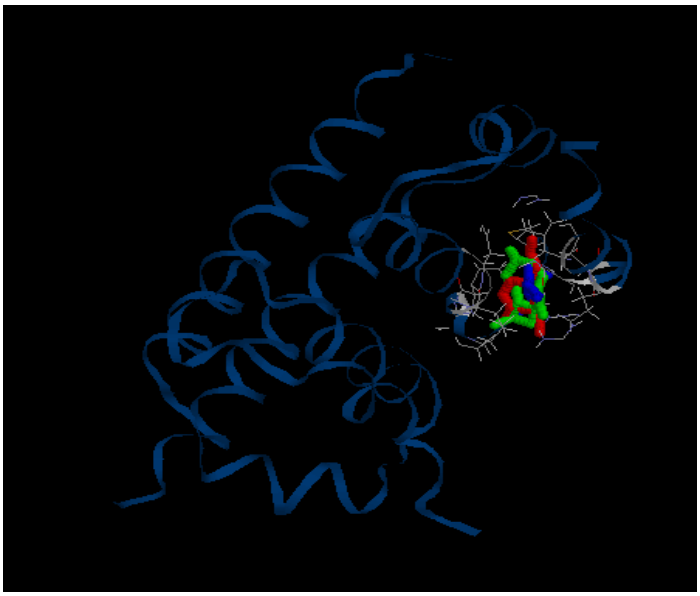

Fig. 9: The Total Binding Energy (kcal/mol) profile for Dengue virus Capsid protein with 3 ligands.

4.3.2. The Total Binding Energy for Dengue virus envelope protein with 3 ligands

From Table – 2, Table – 4 and Table – 6, the docking simulation of 3 ligands were performed for Dengue virus envelope protein. From the docking study, we observed that compound – A has best binding affinity with the target envelope protein with the binding energy value of -71.1 kcal/mol. Interaction analysis of binding mode of compound –A in dengue virus envelope protein reveals that it forms one hydrogen bond with low energy, with Arg(672) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus envelope protein with 3 ligands: is shown in Fig.10.

Fig. 10: The Total Binding Energy (kcal/mol) profile for Dengue virus envelope protein with 3 ligands.

4.4. Structural proteins of Ebola virus

4.4.1. The Total Binding Energy for Ebola virus Nucleoprotein protein with 3 ligands

From Table – 2, Table – 4 and Table – 6, the docking simulation of 3 ligands were performed for Ebola virus Nucleoprotein. From the docking study, we observed that compound – C has best binding affinity with the target Nucleoprotein with the binding energy value of -70.4 kcal/mol. Interaction analysis of binding mode of compound –C in dengue virus Nucleoprotein reveals that it forms one hydrogen bond with low energy, with His(737) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Ebola virus Nucleoprotein with 3 ligands: is shown in Fig.11.

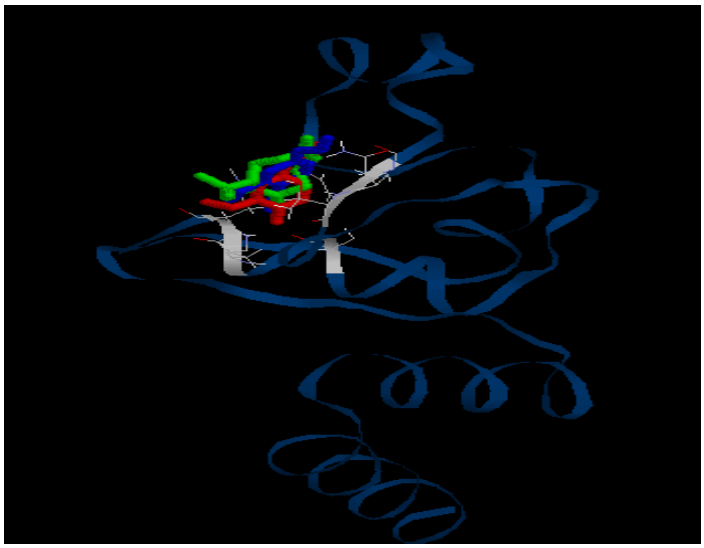

Fig. 11: The Total Binding Energy (kcal/mol) profile for Ebola virus nucleoprotein with 3 ligands.

4.4.2. The Total Binding Energy for Ebola virus VP40 Matrix protein with 3 ligands

From Table – 2, Table – 4 and Table – 6, the docking simulation of 3 ligands were performed for Ebola virus VP40 Matrix protein. From the docking study, we observed that compound – C has best binding affinity with the target VP40 Matrix protein with the binding energy value of -70.1 kcal/mol. Interaction analysis of binding mode of compound –A in dengue virus VP40 Matrix protein reveals that it forms two hydrogen bonds with low energy, with Ala(62) and Arg(137) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Ebola virus VP40 Matrix protein with 3 ligands: is shown in Fig.12.

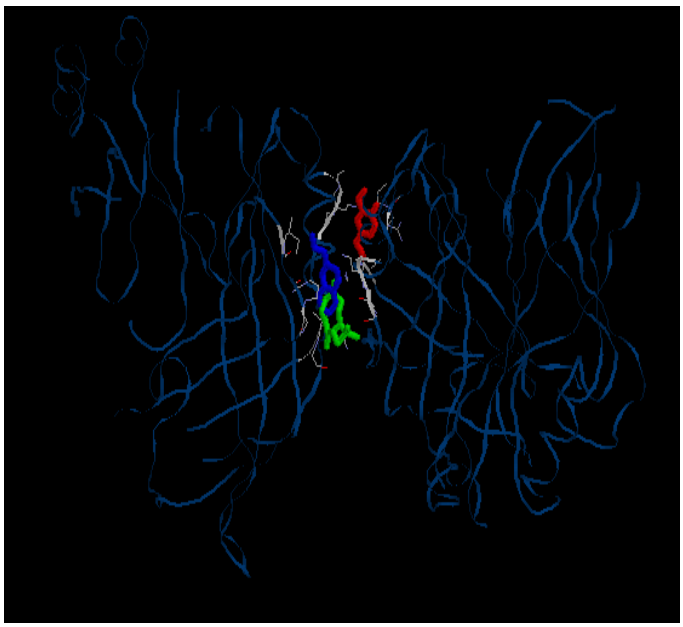

Fig. 12: The Total Binding Energy (kcal/mol) profile for Ebola virus VP40 Matrix protein with 3 ligands.

4.4.3. The Total Binding Energy for Ebola virus VP24 Nucleocaspid protein with 3 ligands

From Table – 2, Table – 4 and Table – 6, the docking simulation of 3 ligands were performed for Ebola virus VP24 Nucleocaspid protein. From the docking study, we observed that compound – A has best binding affinity with the target VP24 Nucleocaspid protein with the binding energy value of -67.2 kcal/mol. Interaction analysis of binding mode of compound – A in dengue virus VP24 Nucleocaspid protein reveals that it forms one hydrogen bond with low energy, with Gln(83) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Ebola virus VP24 Nucleocaspid protein with 3 ligands: is shown in Fig.13.

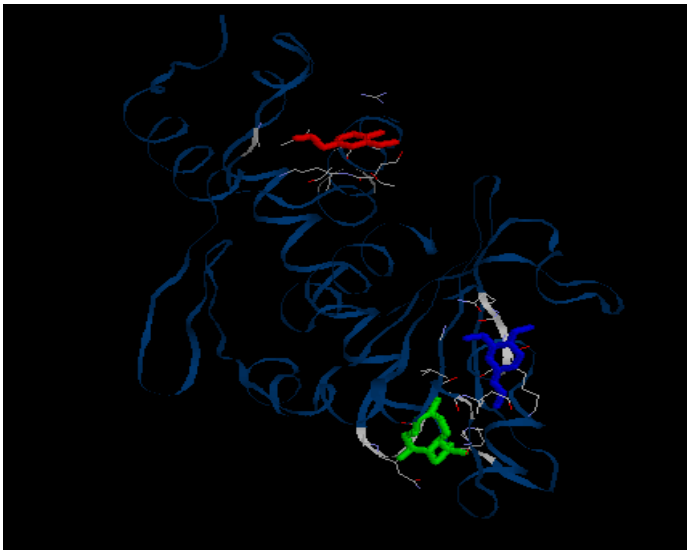

Fig.13: The Total Binding Energy (kcal/mol) profile for Ebola virus VP24 Nucleocaspid protein with 3 ligands.

4.4.4. The Total Binding Energy for Ebola virus glycoprotein with 3 ligands

From Table – 2, Table – 4 and Table – 6, the docking simulation of 3 ligands were performed for Ebola virus NS5 protein From the docking study, we observed that compound –C has best binding affinity with the target glycoprotein with the binding energy value of -91.7kcal/mol. Interaction analysis of binding mode of compound –C in dengue virus glycoprotein reveals that it forms one hydrogen bond with low energy, with Trp (103) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Ebola virus glycoprotein with 3 ligands: is shown in Fig.14.

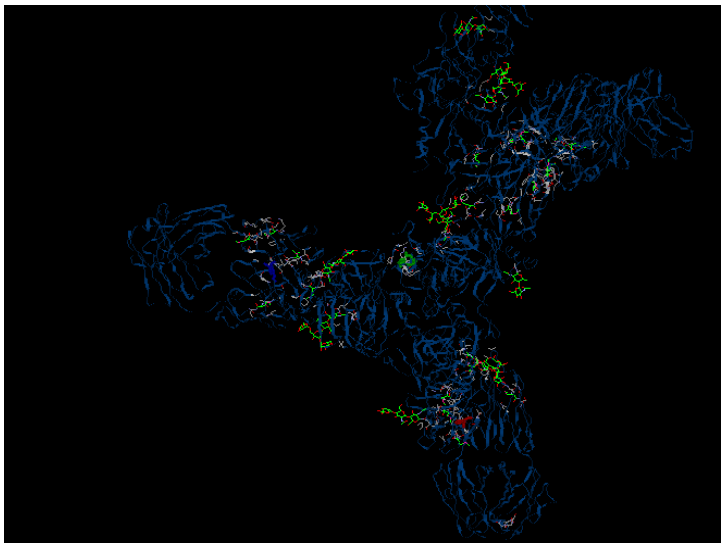

Fig. 14: The Total Binding Energy (kcal/mol) profile for Ebola virus glycoprotein protein with 3 ligands.

5. CONCLUSION

Our molecular docking studies explored the possible binding modes of 3 compounds that are present in *Ocimum sanctum* leaf with seven proteins of Dengue virus and seven proteins of Ebola virus. Dengue virus consists of envelope protein, NS1 protein, Transmembrane doamin of NS2A, NS2B/NS3 protease, NS3 helicase, NS5 protein and capsid protein; Ebola virus consists of Glycoprotein, Nucleoprotein, VP40 Matrix protein, VP24 Nucleocaspid protein, VP35, VP30 and Polymerase L protein. It revealed that all the 3 compounds show minimum affinity with all the proteins. The compound A (Benzene, 1, 2-dimethoxy-4-(1-propenyl)) and compound C (Eugenol) shows best results compared to other compounds. On comparing the binding energy and the binding site residues, we found that all the compounds will 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 A has highest binding affinity with most of the structural proteins of Dengue virus and compound C has the highest binding affinity with majority of the structural proteins of Ebola virus. Whereas the compound C is shown to have highest binding affinity with most of the non structural proteins of Dengue virus and the non structural proteins of Ebola virus has highest binding affinities with both A and C compounds and therefore it can be used as an effective drug target for Dengue virus as well as Ebola virus. Hence, the Compound C may be considered as the effective drug target for both dengue and ebola 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 Ebola.

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