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IN SILICO STUDIES ON DENGUE AND SARS CORONA VIRAL PROTEINS WITH SELECTED *CORIANDRUM SATIVUM* LEAVES CONSTITUENTS

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ABSTRACT

Dengue virus contains seven proteins and SARS Corona virus contains twelve proteins. Recent studies have shown that these proteins are considered to be the most effective for drug designing in humans. Phytochemicals present in *Coriandrum sativum* leaves are found to have anti-inflamatory and antifungal properties. In our study, the binding efficiency of 4 compounds that is present in the *Coriandrum sativum* leaves with all these two viral proteins were performed through Insilico methods. By our virtual screening and molecular docking result, we found that squalene and n-hexadecenoic acid have highest binding affinity with these proteins.

KEYWORDS: *Coriandrum sativum*, squalene, molecular docking, binding affinity.

1. INTRODUCTION

Natural products derived from plants for the treatment of diseases have proved that nature stands a golden mark to show relationship between man and his environment. The researches and utilization of herbal medicine in the treatment of diseases increases everyday. Medicinal plants are believed traditionally to be a therapeutic agent for the treatment of many diseases.[1,2] *Coriandrum sativum* which is commonly called as coriander or cilantro is packed with bunch of health and medicinal benefits. Due to which numerous nutritional values, it is also regarded as Wonder Herb of the world. It is full of phytonutrients, antioxidants, essential oils, antiseptic analgesic, aphrodisiac, fungicidal, natural stimulant, etc. It has adequate amount of vitamin A, C and K including with many essential oils and acids.[3] The acids present in *Coriandrum sativam* leaves like linoleic acid, oleic acid, palmitic acid, stearic acid and ascorbic acid are effective in reducing cholesterol levels in the blood. It is also increasingly popular as a means of preventing nausea, vomiting, and stomach disorders.[4]

GC-MS chromatogram of the methanolic extract of *Coriandrum sativum* leaves showed four major peaks, n-Hexadecanoic acid, Squalene, 9,12 –octadecadedienoic acid (Z,Z) and 9,12 octadecadienoic acid (Z,Z)-2-hyroxy-1-(hydroxy methyl) ethyl ester 2,3-dihydoxy propyl ester were the major components in the extract. Squalene has the property of Antimicrobial, Antioxidant, Antitumor agent, potential uses in cosmetic dermatology. n -Hexadecanoic acid is widely known for its anti-inflammatory and Antimicrobial activity.[5] 9, 12 octadecadienic acid is known for its hepatoprotective, Antihistaminic, hypocholesterolemic, Anti-eczemic properties.[6] 9, 12 octadecadienoic acid (Z, Z)-2-hyroxy-1-(hydroxy methyl) ethyl ester 2,3-dihydoxy propyl ester is known for its hepato protective, Antihistaminic, hypocholesterolemic, Anti-eczemic, Antibacterial, Antimicrobial activity and is used as antibiotic.[7,8]

Dengue is caused by Dengue virus (DENV), a mosquito-borne flavivirus. DENV is a single stranded RNA positive-strand virus of the family Flaviviridae, genus Flavivirus. This genus includes also the West Nile virus positive-strand virus of the family Flaviviridae, genus Flavivirus.[9] This genus includes also the West Nile virus Tick-borne Encephalitis Virus, Yellow Fever Virus, and several other viruses which may cause encephalitis. DENV causes a wide range of diseases in humans, from a self limited Dengue Fever (DF) to a life-threatening syndrome called Dengue Hemorrhagic Fever (DHF) or Dengue Shock Syndrome (DSS).[10]

The antigenically four different serotypes of the virus are DENV-1, DENV-2, DENV-3, DENV-4.There are 180

identical copies of the envelope (E) protein attached to the surface of the viral membrane by a short transmembrane segment.[11] The virus has a genome of about 11000 bases that encodes a single large polyprotein that is subsequently cleaved into several structural and non-structural mature peptides. As an endemic disease, dengue occurs regularly in subtropical and tropical regions of the world, and approximately 40% of people live in regions of the world where there is a risk of contracting it. The mosquito, which needs regular meals of blood to mature its eggs, completes the cycle by biting a healthy human, transmitting the disease in one act.[12] Capsid protein of dengue virus is a highly basic protein of 12kDa that forms homodimers in solution with affinity for both nucleic acids and lipid membranes. The mature capsid protein remains associated with ER membranes via hydrophobic region, which is conserved in a wide range of mosquitos.[9] Envelope protein is a class two fusion protein, essential for receptor binding, membrane fusion, and inducing protective antibodies. This protein folds into three distinct domains (D1, D2 and D 3) that co-relate to the antigenic domains.[13] Once the cells are infected with dengue virus, it encodes a non- structural protein 1 (NS1), a relatively conserved 45-50kDa glycoprotein. Then NS1 is secreted from the mammalian cells as soluble hexamer.NS1 in their folded state serve to deliver optimal antigencity.[14] Dengue virus NS2A protein is essential for viral replication and is poorly characterized by membrane protein. It displays both protein-protein and protein-membrane interactions this may be involved in membrane rearrangements. NS2B\NS3 protease is translated as a single polyprotein precursor, which must be cleaved into individual proteins by host protease. This step of cleavage is obligate step of viral life cycle [15]. NS3 helicase protein is Mg^{2+} dependent and responsible for replication by unwinding the duplex RNA utilizing the chemical energy derived by ATP hydrolysis. Non structural protein 5 (NS5) consists of methyl transferase and RNA dependent RNA polymerase domains catalyze methylation and replication.[16,17]

SARS coronavirus, also known as SARS-CoV is a virus which can cause Severe Acute Respiratory Syndrome (SARS).SARS corona viruses are single stranded, positive sense RNA viruses which belongs to the family Coronaviridae[18] . Coronaviruses can cause a range of symptoms varying from common cold to serious respiratory illness. The symptoms include rhinorrhea, sneezing, cough, bronchitis and so on. There are three groups of coronaviruses: alpha, beta, gamma. Structural proteins include spike glycoprotein(S), membrane protein(M), envelope protein(E), nucleocapsid protein(N). Spike glycoprotein is composed of 1255 amino acids long, its carboxy terminal is composed of the transmembrane region and cytoplasmic tail. It has two functional domains S^1 and S^2.[19] Membraneproteinis a transmembrane glycoprotein and plays a significant role in virus specific humoral response and is able to elicit efficient neutralizing antibodies. Envelope protein is a small integral membrane protein of 76 amino acid, contains a short hydrophilic amino terminus followed by a hydrophobic region and a hydrophilic carboxy terminus. The envelope (E) protein from coronaviruses is a small polypeptide that contains at least one alpha-helical transmembrane domain. Absence, or inactivation, of E protein results in attenuated viruses, due to alterations in either virion morphology or tropism. Apart from its morphogenetic properties, protein E has been reported to have membrane permeabilizing activity.[20] Coronavirus N proteins share the same modular organization. Structures of SARS-CoV N protein provide insight into nucleocapsid formation. Nucleocapsid protein binds to nucleic acid at multiple sites in a coupled-allosteric manner. Spike glycoprotein mediates fusion of the virion and cellular membranes by acting as a class I viral fusion protein. Under the current model, the protein has at least three conformational states: pre-fusion native state, pre-hairpin intermediate state, and post-fusion hairpin state. During viral and target cell membrane fusion, the coiled coil regions (heptad repeats) assume a trimer-of-hairpins structure, positioning the fusion peptide in close proximity to the C-terminal region of the ectodomain. Membrane proteincomponent of the viral envelope that plays a central role in virus morphogenesis and assembly via its interactions with other viral proteins.[21]

Bioinformatics is an interdisciplinary field mainly involves genetics, molecular biology, mathematics, statistics which addresses the biological problems in the computational point of view.[22] The Protein Data Bank (PDB) which is the single global repository for experimentally 262determined 3D structures of biological macromolecules and their complexes with ligands which consists of >130000 structures determined by macromolecular crystallography, NMR and electron cryo-microscopy.[23] Recently developed wwPDB tool for deposition, validation of biological macromolecules which allows efficient and effective usage by research scientists, students and the curious public world wide. 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.[24]

2. MATERIALS AND METHODOLOGIES

2.1. Preparation of 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 SARS Corona virus were used for this study. The 3D structure of all the nineteen proteins were downloaded from PDB and saved in PDB format. The downloaded proteins were viewed in Py-Mol viewer.[25]

2.2. Preparation of ligands

Ligands selected were from the previous studies on GCMS analysis on *Coriandrum sativum* extract. 4 ligands were used for the study. Ligands were constructed using ChemSketch [26]. 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, C and D 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 [27]. 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.[28]

3. RESULTS

3.1. Total Binding Energy (kcal/mol) profile for Dengue and SARS Coronaviruses proteins with 4 ligands

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

Ligand	Compound name	Dengue Virus					SARS Corona Virus					
		NS1 protein	Trans membrane domain of NS2A	NS2B / NS3 protease	NS3 helicase	NS5 protein	NS1protein	NS3 protein	NS7 protein	NS9 protein	NS10 protein	NS15 protein
A	n – hexadecenoic acid	-77.8	-78.7	-73.9	-82.1	-84.1	-76.1	-69.0	-72.4	-80.2	-83.4	-83.0
B	9,12, octadecadienoic acid	-85.9	-80.3	-84.0	-87.4	-83.0	-94.4	-84.5	-82.1	-91.2	-79.3	-81.0
C	Squalene	-95.2	-94.4	-98.8	-96.7	-107	-89.5	-103.3	-94.5	-99.8	-100	-101.1
D	9,12, octadecadienoic acid,2, hydroxy, 1(hydroxy methyl)ethyl ester, 2,3 dihydroxy propyl ester	-73.9	-85.0	-92.4	-95.0	-88.9	-93.7	-91.8	-77.0	-88.8	-85.9	-88.6

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

Ligand	Compound name	Dengue virus		SARS Corona virus			
		Capsid protein	Envelope protein	Envelope protein	Nucleocapsid protein	Spike glycoprotein	Membrane protein
A	n – hexadecenoic acid	-76.3	-72.2	-85.9	-82.9	-98.4	-75.7
B	9,12, octadecadienoic acid	-82.5	-84.2	-95.3	-83.0	-85.8	-86.1
C	Squalene	-97.7	-101.6	-103.8	-99.3	-86.8	-95.6
D	9,12, octadecadienoic acid,2, hydroxy, 1(hydroxy methyl) ethyl ester, 2,3 dihydroxy propyl ester	-90.1	-93.8	-94.2	-89.3	-85.2	-99.8

3.2. H – Bond profile for Dengue and SARS Corona viruses protein with 4 ligands

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

Ligand	Compound name	Dengue Virus					SARS Corona Virus					
		NS1 protein	Trans membrane domain of NS2A	NS2B / NS3 protease	NS3 helicase	NS5 protein	NS1protein	NS3 protein	NS7 protein	NS9 protein	NS10 protein	NS15 protein
A	n – hexadecenoic acid	-	H-M	H-M	H-S	H-M	-	-	-	H-M H-S	-	-
B	9,12, octadecadienoic acid	H-S	H-M H-S	H-M H-S	H-M	H-M	H-S	H-M H-S	H-S	H-M	H-S H-M	H-M H-S
C	Squalene	-	-	-	-	-	-	-	-	-	-	-
D	9,12, octadecadienoic acid,2, hydroxy, 1(hydroxy methyl)ethyl ester, 2,3 dihydroxy propyl ester	H-M	H-M	H-M	H-S	H-S	H-S H-M	H-M	H-S	H-S	H-S H-M	H-M H-S

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

Ligand	Compound name	Dengue virus		SARS Corona virus			
		Capsid protein	Envelope protein	Envelope protein	Nucleocapsid protein	Spike glycoprotein	Membrane protein
A	n – hexadecenoic acid	-	-	-	H-S	H-S	H-S
B	9,12, octadecadienoic acid	H-M	H-M	H-S	H-M	-	H-S H-M
C	Squalene	-	-	-	-	-	-
D	9,12, octadecadienoic acid,2, hydroxy, 1(hydroxy methyl) ethyl ester, 2,3 dihydroxy propyl ester	H-M	H-M	-	H-M	H-S	H-S

3.3. Amino acid position profile for Dengue and SARS Corona virus protein with 4 ligands.

Table 5: Amino acid position profile for Dengue and SARS Corona virus non- structural proteins with 4 ligands.

Ligand	Compound name	Dengue Virus					SARS Corona Virus					
		NS1 protein	Trans membrane domain of NS2A	NS2B / NS3 protease	NS3 helicase	NS5 protein	NS1protein	NS3 protein	NS7 protein	NS9 protein	NS10 protein	NS15 protein
A	n – hexadecenoic acid	-	Gly (3)	Ala (165)	Asn (481)	Glu (40),Ala (41)	-	-	-	Ser (59)	-	-
B	9,12, octadecadienoic acid	Asp (180)	Ile (2)	Lys (74),Asn (167)	Lys (515)	Lys (105)	Arg (62)	Phe (6), Lys (63)	Ser (59)	Val (41)	Lys (46)	Lys (70), Asp (296)
C	Squalene	-	-	-	-	-	-	-	-	-	-	-

D	9,12, octadecadienoic acid,2, hydroxy, 1(hydroxy methyl) ethyl ester, 2,3 dihydroxy propyl ester	Lys (223)	Phe (15)	Asn (167)	Thr (450)	His (53)	Ser (63**)**	Ile (39)	Ser (63)	Arg (39)	Thr (49)	Lys (89)

Table 6: Amino acid position profile for Dengue and SARS Corona virus structural proteins with 4 ligands.

Ligand	Compound name	Dengue virus		SARS Corona virus			
		Capsid protein	Envelope protein	Envelope protein	Nucleocapsid protein	Spike glycoprotein	Membrane protein
A	n – hexadecenoic acid	-	-	-	Arg (320)	Asn (721)	Arg (181)
B	9,12, octadecadienoic acid	Leu (38)	Met (580)	Thr (30)	Phe (275)	-	Ser (11)
C	Squalene	-	-	-	-	-	-
D	9,12, octadecadienoic acid,2, hydroxy, 1(hydroxy methyl)ethyl ester, 2,3 dihydroxy propyl ester	Gly (70)	Arg (627)	-	Gly (276)	Arg (758)	Arg (170)

4. DISCUSSION

Considering all the tables from Table – 1, to Table - 6, the 3D structure coordinates of seven proteins of dengue and ten proteins of SARS Corona viruses are optimized and 4 compounds from *Coriander sativum* leaves extract are identified. The total binding energy of the compounds with all the seventeen proteins was calculated using iGEMDOCK. Evaluations of binding conformation of these 4 compounds with seven dengue as well as SARS Corona 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 SARS Corona 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 "C" is found to have lower ligand binding energy (binding energy value = -101.6 kcal/mol), than other analogs for Envelope protein. Compound "C" has least binding energy score with capsid protein (binding energy value -97.7 kcal/mol), the structural proteins of SARS Corona virus had following binding energies, Nucleocapsid protein ('C' binding energy value -99.3kcal\mol), Envelope protein('C' binding energy value -103.8kcal\mol), Membrane protein('D', binding energy value -99.8kcal\mol), Spike Glycoprotein('A', binding energy value -98.4kcal\mol). The non- structural proteins of Dengue virus had these binding energy values: Trans membrane domain of NS2A ('C', binding energy value -94.45kcal/mol), NS2B / NS3 protease ('C', binding energy value -98.84kcal/mol), NS3 helicase ('C', binding energy value -96.78kcal/mol), NS5 protein ('C', binding energy value -107kcal/mol) and NS1 protein ('C', binding energy value -95.2kcal/mol). And the non- structural proteins of SARS Corona virus have, NSP1 ('B', binding energy value -94.44 kcal/mol), NSP3 ('C', binding energy value -103.3 kcal/mol), NSP7 ('C', binding energy values -94.5 kcal/mol), NSP9 ('C ,binding energy values -99.82 kcal/mol), NSP10('C', binding energy values -100.02 kcal/mol), NSP15('C', binding energy values -101.11 kcal/mol).We further analyzed the docked pose for finding the binding mode of compound "A", and compound "C" in to seven dengue and ten SARS Corona 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 – C has best binding affinity with the target NS1 protein with the binding energy value of -95.2 kcal/mol. 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.

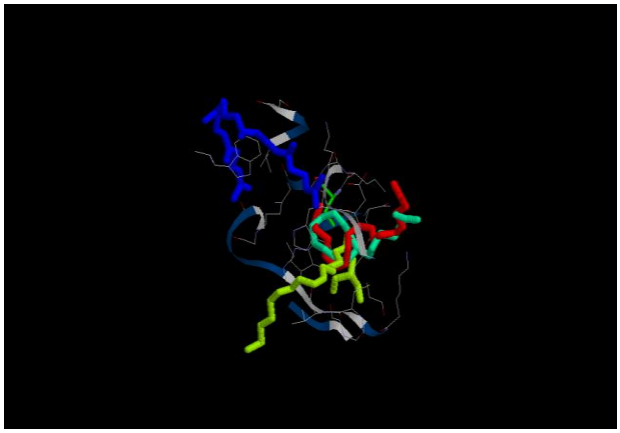

Fig. 1: The Total Binding Energy for Dengue virus NS1 protein with 4 ligands.

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 membranedomain of NS2A. From the docking study, we observed that compound – C has best binding affinity with the target Trans membrane domain of NS2A with the binding energy value of -94.45 kcal/mol. 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.

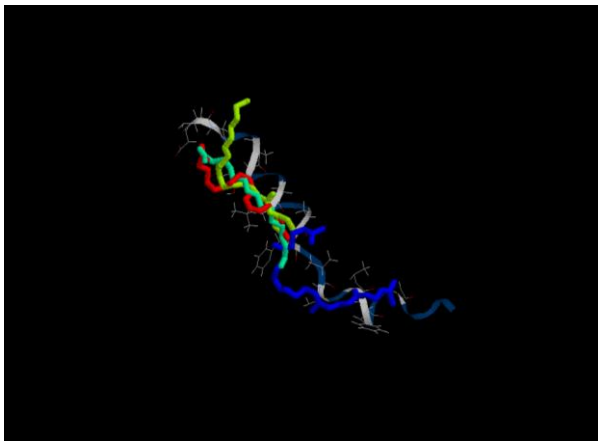

Fig. 2: The Total Binding Energy for Dengue virus Trans membrane domain of NS2A with 4 ligands

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 / NS3protease. From the docking study, we observed that compound – C has best binding affinity with the target NS2B / NS3protease with the binding energy value of -98.84kcal/mol. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus NS2B / NS3protease with 4 ligands: is shown in Fig.3.

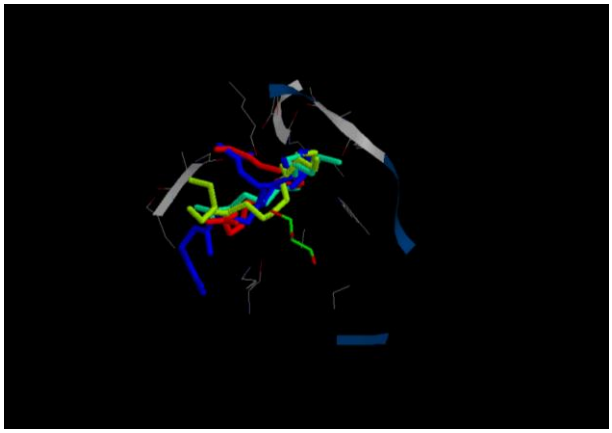

Fig. 3: The Total Binding Energy for Dengue virus NS2B / NS3 protease with 4 ligands.

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 NS3helicase. From the docking study, we observed that compound – C has best binding affinity with the target NS3helicase with the binding energy value of -96.78 kcal/mol. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus NS3helicase with 4 ligands: is shown in Fig.4.

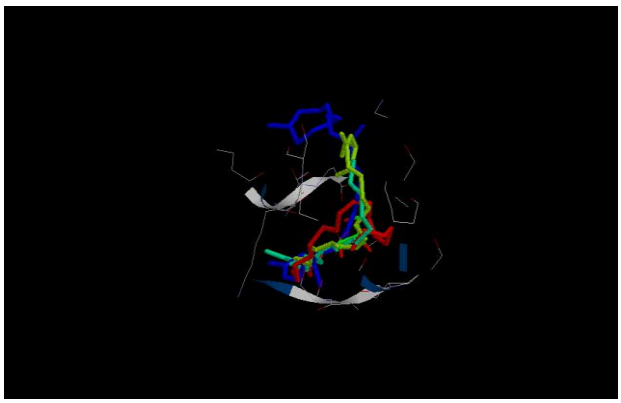

Fig. 4: The Total Binding Energy for Dengue virus NS3 helicase with 4 ligands.

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 virusNS5 proteinFrom the docking study, we observed that compound – C has best binding affinity with the target NS5 protein with the binding energy value of -107kcal/mol. 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

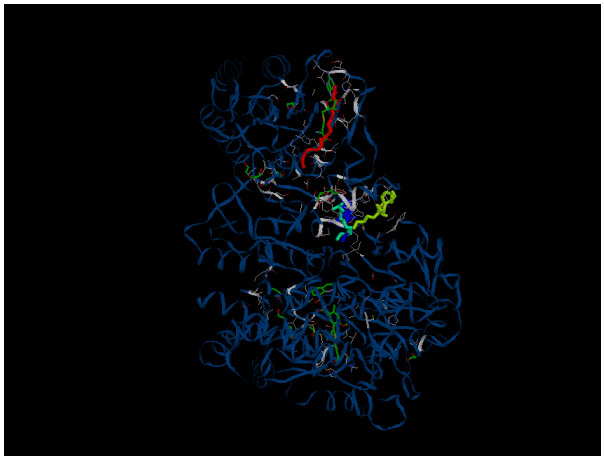

Fig. 5: The Total Binding Energy for Dengue virus NS5 protein with 4 ligands.

4.2. Non-Structural proteins of SARS Corona Virus

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

From Table – 1, Table – 3 and Table – 5, the docking simulation of 3 ligands were performed for SARS Corona virus NS1 protein. From the docking study, we observed that compound – B has best binding affinity with the target NS1 protein with the binding energy values of -94.44 kcal/mol. A close-up view of the Total Binding Energy (kcal/mol) profile for SARS Corona virus NS1 protein with 4 ligands: is shown in Fig.6.

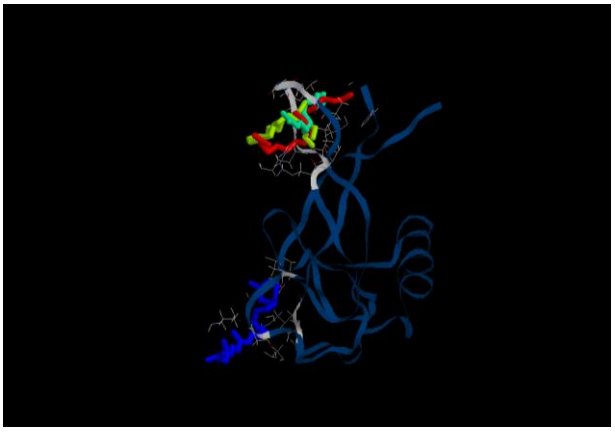

Fig. 6: The Total Binding Energy for SARS Corona virus NS1 protein with 4 ligands.

4.2.2. The Total Binding Energy for SARS Corona virus NS3 protein with 4 ligands

From Table – 1, Table – 3 and Table – 5, the docking simulation of 4 ligands were performed for SARS Corona virusNS3 protein**.** From the docking study, we observed that compound – C has best binding affinity with the target NS3 protein with the binding energy value of -103.3kcal/mol. A close-up view of the Total Binding Energy (kcal/mol) profile for SARS Corona virus NS3 protein with 4 ligands: is shown in Fig.7.

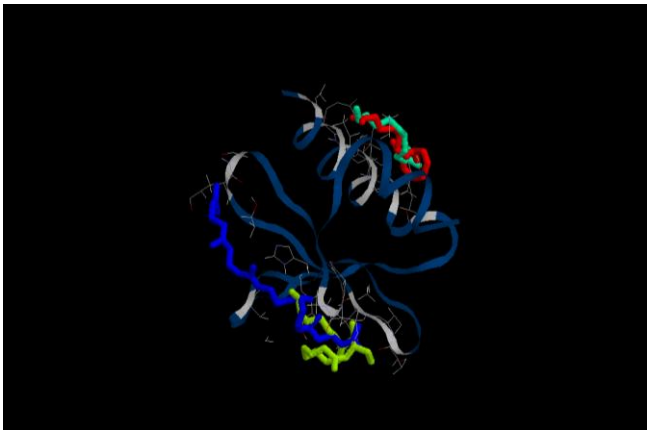

Fig. 7: The Total Binding Energy for SARS Corona virus NS3 protein with 4 ligands.

4.2.3. The Total Binding Energy for SARS Corona virus NS7 protein with 4 ligands

From Table – 1, Table – 3 and Table – 5, the docking simulation of 4 ligands were performed for SARS Corona virus NS7 protein. From the docking study, we observed that compound – C has best binding affinity with the target NS7 protein with the binding energy value of -94.58kcal/mol. A close-up view of the Total Binding Energy (kcal/mol) profile for SARS Corona virus NS7 protein with 4 ligands: is shown in Fig.8.

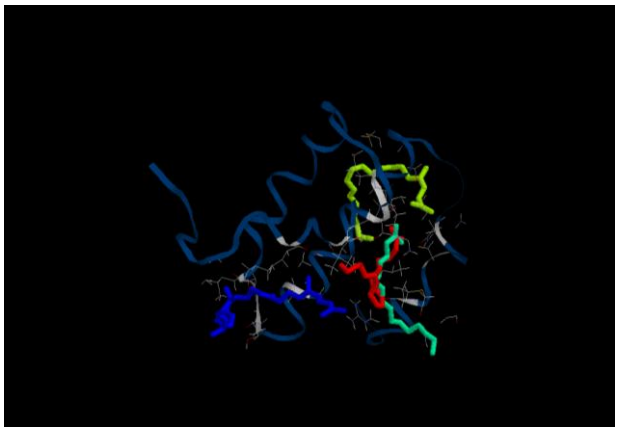

Fig. 8: The Total Binding Energy for SARS Corona virus NS7 protein with 4 ligands.

4.2.4. The Total Binding Energy for SARS Corona virus NS9 protein with 4 ligands

From Table – 1, Table – 3 and Table – 5, the docking simulation of 4 ligands were performed for SARS Corona virus ns protein. From the docking study, we observed that compound – C has best binding affinity with the target NS9 protein with the binding energy value of -99.8 kcal/mol.A close-up view of the Total Binding Energy (kcal/mol) profile for SARS Corona virus NS9 protein with 4 ligands: is shown in Fig.9.

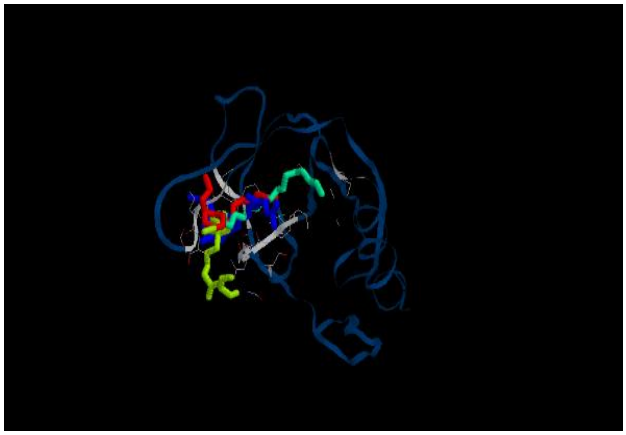

Fig. 9: The Total Binding Energy for SARS Corona virus NS9 protein with 4 ligands.

4.2.5. The Total Binding Energy for SARS Corona virus NS10 protein with 4 ligands:

From Table – 1, Table – 3 and Table – 5, the docking simulation of 4 ligands were performed for SARS Corona virusNS10 protein. From the docking study, we observed that compound – C has best binding affinity with the target NS10 protein with the binding energy value of -100.07 kcal/mol. A close-up view of the Total Binding Energy (kcal/mol) profile for SARS Corona virus NS10 protein with 4 ligands: is shown in Fig.10.

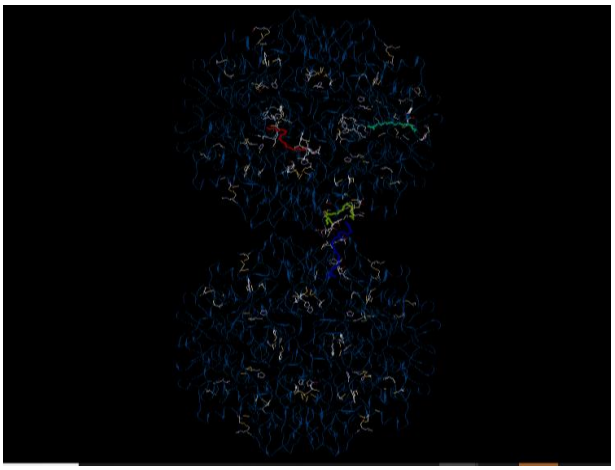

Fig. 10: The Total Binding Energy for SARS Corona virus NS10 protein with 4 ligands.

4.2.6. The Total Binding Energy for SARS Corona virus NS15 protein with 4 ligands

From Table – 1, Table – 3 and Table – 5, the docking simulation of 4 ligands were performed for SARS Corona virus NS15 protein. From the docking study, we observed that compound – C has best binding affinity with the target NS15 protein with the binding energy value of -101.11 kcal/mol. A close-up view of the Total Binding Energy (kcal/mol) profile for SARS Corona virus NS15 protein with 4 ligands: is shown in Fig.11.

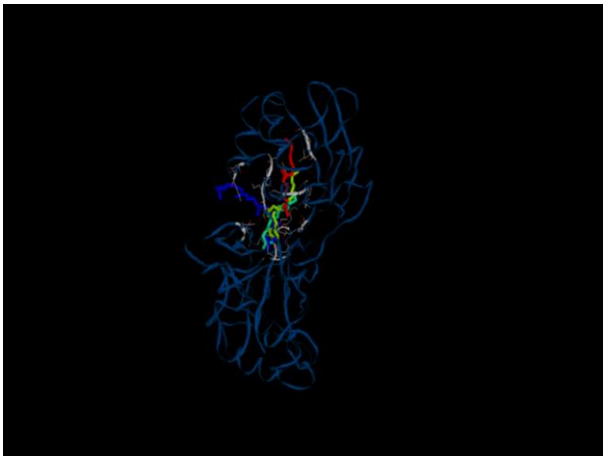

Fig. 11: The Total Binding Energy for SARS Coronavirus NS15 protein with 4 ligands.

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 – C has best binding affinity with the target Capsid proteinwith the binding energy value of -97.7 kcal/mol. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus Capsid protein with 4 ligands: is shown in Fig.12.

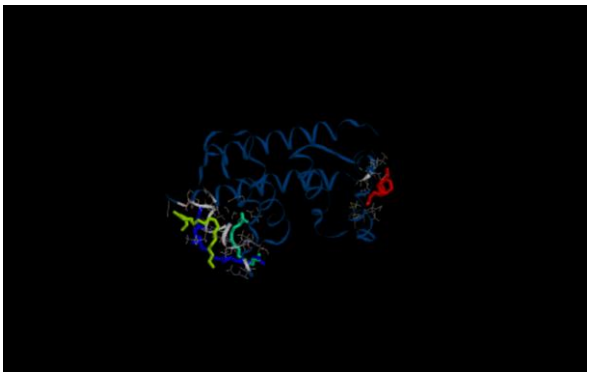

Fig. 12: The Total Binding Energy for Dengue virus Capsid protein with 4 ligands.

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 – C has best binding affinity with the target envelope protein with the binding energy value of -101.6 kcal/mol.A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus envelope protein with 4 ligands: is shown in Fig.13.

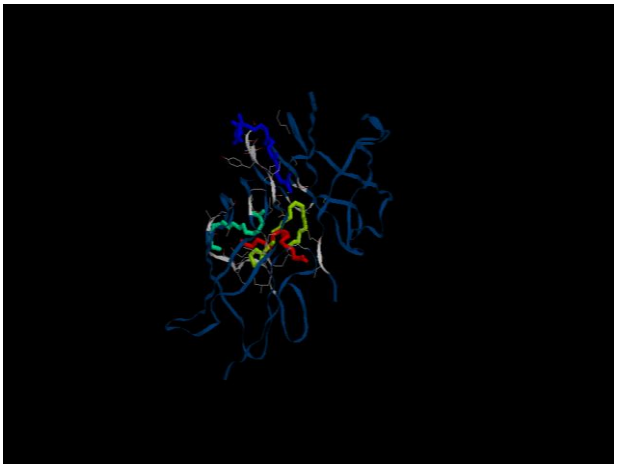

Fig. 13: The Total Binding Energy for Dengue virus envelope protein with 4 ligands.

4.4. Structural proteins of SARS Corona virus

4.4.1. The Total Binding Energy for SARS Corona virus Envelope protein with 4 ligands

From Table – 2, Table – 4 and Table – 6, the docking simulation of 4 ligands were performed for SARS Corona virus Envelope protein. From the docking study, we observed that compound – C has best binding affinity with the target Envelope protein with the binding energy value of -103.8 kcal/mol. A close-up view of the Total Binding Energy (kcal/mol) profile for Ebola virus Envelope protein with 4 ligands: is shown in Fig.14.

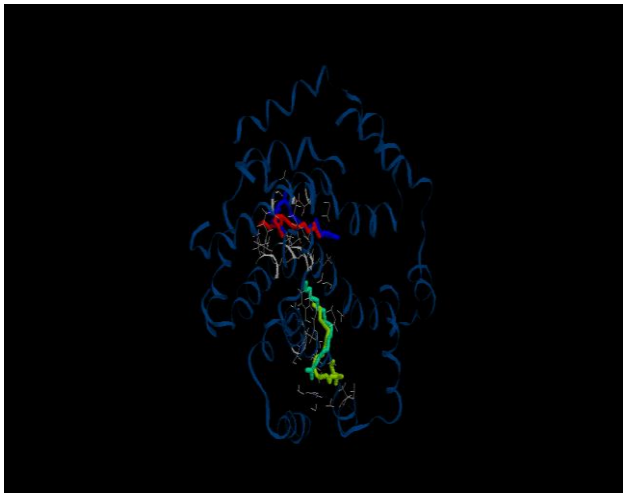

Fig. 14: The Total Binding Energy for SARS Corona virus Envelope protein with 4 ligands.

4.4.2. The Total Binding Energy for SARS Corona virus Nucleocapsid protein with 4 ligands

From Table – 2, Table – 4 and Table – 6, the docking simulation of 4 ligands were performed for SARS virus Nucleocapsid protein. From the docking study, we observed that compound – C has best binding affinity with the target Nucleocapsid protein with the binding energy value of -99.3kcal/mol. A close-up view of the Total Binding Energy (kcal/mol) profile for SARS Corona virus nucleocapsid protein with 4 ligands: is shown in Fig.15

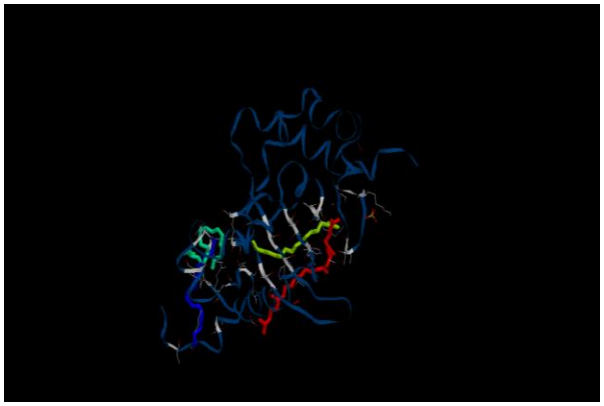

Fig. 15: The Total Binding Energy for SARS Corona virus nucleocapsid protein with 4 ligands.

4.4.3. The Total Binding Energy for SARS Corona virus Spike glycoprotein with 4 ligands

From Table – 2, Table – 4 and Table – 6, the docking simulation of 4 ligands were performed for SARS Corona virusspike glycoprotein**.** From the docking study, we observed that compound –A has best binding affinity with the target glycoprotein with the binding energy value of -98.4kcal/mol. Interaction analysis of binding mode of compound –A in SARS Corona virus spike glycoprotein reveals that it forms one hydrogen bond with low energy, with Asn(721) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for SARS Corona virus spike glycoprotein with 4 ligands: is shown in Fig.16.

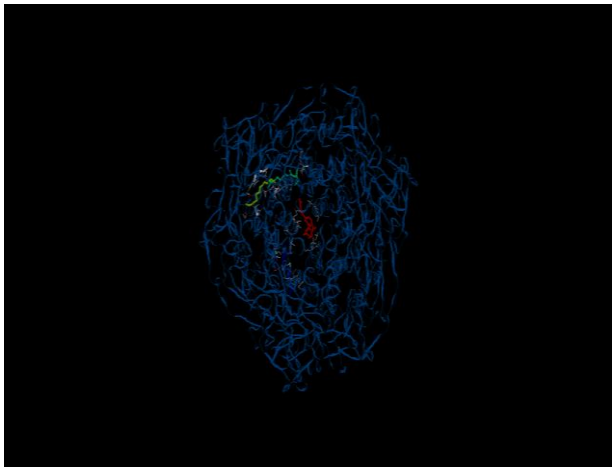

Fig. 16: The Total Binding Energy for SARS Corona virus spike glycoprotein with 4 ligands.

4.4.4. The Total Binding Energy for SARS Corona virus Membrane protein with 4 ligands

From Table – 2, Table – 4 and Table – 6, the docking simulation of 4 ligands were performed for SARS Corona virus membrane protein. From the docking study, we observed that compound – D has best binding affinity with the target membrane protein with the binding energy value of -99.8 kcal/mol. Interaction analysis of binding mode of compound –D in SARS Corona virus membrane protein reveals that it forms one hydrogen bond with low energy, with Arg(170) residue. A close-up

view of the Total Binding Energy (kcal/mol) profile for SARS Corona virus membrane protein with 4 ligands: is shown in Fig.17.

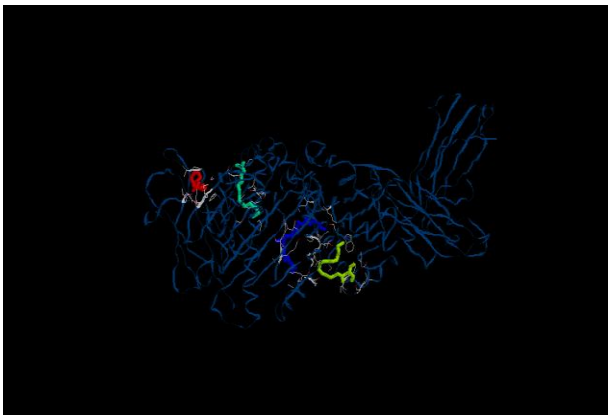

Fig. 17: The Total Binding Energy (kcal/mol) profile for SARS Corona virus membrane protein with 4 ligands.

5. CONCLUSION

Our molecular docking studies explored the possible binding modes of 4 compounds that are present in *Coriandrum sativum* with seven proteins of Dengue virus and ten proteins of SARS Corona virus. Dengue virus consists of envelope protein, NS1 protein, Transmembrane domain of NS2A, NS2B/NS3 protease, NS3 helicase, NS5 protein and capsid protein; SARS Corona virus consists of Spike glycoprotein, Nucleocapsid protein, envelope protein, membrane protein, NS1, NS3, NS7, NS9, NS10 and NS15 proteins. It revealed that all the 4 compounds show minimum affinity with all the proteins. The compound C (Squalene) 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 C 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 SARS Corona 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 SARS Corona virus has highest binding affinities with C compound and therefore it can be used as an effective drug target for Dengue virus as well as SARS Corona virus. Hence, the Compound C may be considered as the effective drug target for both dengue and SARS Corona 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 SARS.

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