WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES
SJIF Impact Factor 7.421
Volume 7, Issue 12, 970-989 Research Article ISSN 2278 – 4357

IN SILICO STUDIES ON DENGUE AND MERS CORONAVIRUS PROTEINS WITH SELECTED *CORIANDRUM SATIVUM* L. HERB CONSTITUENTS

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Article Received on
12 October 2018,

Revised on 02 Nov. 2018,
Accepted on 23 Nov. 2018,

DOI: 10.20959/wjpps201812-12821

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ABSTRACT

Dengue virus contains seven proteins and MERS coronavirus contains six proteins which are considered to be the most effective for drug designing. Phytochemicals present in *Coriandrum sativum* L. function as aromatizing agents and has relaxant activity in the alimentary tract. They are found to have great antibacterial and anticancerous properties. In this study, the binding efficiency of 4 compounds present in the *Coriandrum sativum* L. with all the thirteen proteins of dengue as well as MERS corona virus were performed through In silico methods. By our virtual screening and molecular docking result, we found that Dodecanal has the highest binding affinity with all the viral proteins.

KEYWORDS: Coriander, molecular docking, Phytochemicals, Dodecanol.

1. INTRODUCTION

Medicinal plants have always been in the forefront for their role in the development of human culture. Medicinal plants have always had a dominant role in health care systems where herbal medicine has been used since ages.[1] It is an important element of indigenous medical systems all over the world. The ethno botany provides a rich resource for research and development of natural drugs.[2] Among all the plants *Coriandrum sativum* L, also called as

coriander (kitchen herb) plays a great role for its therapeutic uses. Coriander in the language of Sanskrit is called as "Dhanyaka" which is said to have Carminative and Antihelmintic properties. *Coriandrum sativum* L belonging to family *Apiaceae* is very important for their nutritional and medicinal properties.[3] *Coriandrum sativum* has two varieties i.e. vulgare and microcaprum, the former has larger fruits (3 – 5mm diameter) while the later has smaller fruits (1.5 – 3mm). Their chemical composition varies among different parts of the same plant.[4] *Coriander sativum* plants are considered as one of the most important source of medicine and drugs with many secondary metabolites and essential oils and they are utilised as formulations for health benefits.[7] They are recommended for treatment of alzeihmer's, cancer, dysentery, indigestion, parasitic disease, insomnia, skin disorders, rheumatism, menstrual disorders etc.[5,6] Apart from that *Coriandrum sativum* also shows some anticancerous, antibacterial,antifungal, anticonvulsant, neuroprotactive, hypotensive, hypolipidemic, antidiabetic, analgesic, antioxidant and anti-spoilage properties.[3,5,6]

GC-MS chromatogram of the hydro distilled extract of *Coriandrum sativum* L herb showed four major peaks Dodecanal (Synonym: Lauraldehyde), E-2- Dodecanol (Synonym:Dodecan-2-ol), Decanal (synonym: Decylaldehyde) and E-2-Decenol (synonym: Trans-2-Decen-1-ol) were the major components in the extract. Decanal has the property of Antifungal activity, Aromatic activity and Antimicrobial activity. E-2-Decenol is widely used as a food additive, and has antifungal activities. E-2-Dodecanol is reported to have flavour enhancing properties and is popularly used as fragnance agents; Dodecanal is also used as a flavouring agent.[8]

Dengue, a haemorrhagic fever,[9] is caused due to all four serotypes of dengue virus (DENV-1, DENV-2, DENV-3 and DENV-4).[10] These viruses contain ten proteins out of which three are structural proteins and seven are non structural proteins.[11] 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 an important enzyme for the viral replication process as it is a hetero dimeric protein of NS2B and NS3 protein.[12] The N-terminal of the NS3 protein forms association with the NS2B cofactor which is crucial for the viral replication. NS2B/ NS3 protease has an important role in the viral life cycle.[13] Envelope protein is a structural protein which has a major role in the viral assembly. The protein which is utilised for this 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.[14] The capsid protein is one of the structural proteins, which has a

major function 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).[15] 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.[16] NS3 helicase belongs to the non-structural and a multi-domain dengue virus replication protein.[17] 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 plays a crucial part in the replication of the viral genome. RNA is synthesized via "de novo" by NS5 protein.[18]

MERS coronavirus is a zoonotic virus that causes a Middle East Respiratory Syndrome (MERS) in humans and nonhuman primates and bats have appeared to be the natural host.[19] The MERS and the SARS coronavirus belong to the Coronaviridae family that are novel positive–sense, single stranded RNA viruses of the genus Beta coronavirus. There are six types of Human Coronaviruses, among which the two—the MERS-CoV and the SARS-CoV have shown to cause respiratory disease in both humans and nonhuman primates, with the MERS progressing to acute kidney failure proving to be fatal at 37% mortality rate.[20] The genome of the corona virus is approximately 30 kb long which has a 5' cap and a 3'poly A tail.[21] The genome encodes 10 proteins: two replicase polyproteins (Open Reading Frames[ORFs]1ab and 1a), three structural proteins (Envelope protein, Nucleocapsid protein and Membrane protein), a surface (spike) glycoprotein (S) and five non structural proteins (ORFs 3,4a,4b and 5).[22] Nucleocapsid has a distinct function in replication and viral host interactions as well as it suppress RNAi trigged by siRNAs in mammalian cells.[21,23] The Spike glycoprotein(S protein) is a structural component of the virion membrane and the S1 domain mediates binding to DPP4 host receptor.[24] The non structural protein 3[NSP 3] is classified under hydrolases and has ADRP activity, promotes cytokine expression, RNA directed 5'-3' RNA polymerase activity and cysteine type peptidase activity. NSP 5 plays an important role in the viral protein processing and cleaving of the viral proteins. NSP 13 is classified under hydrolase and has an important function in encoding RNA helicase domain and RNA 5'-triphosphate activity.[21] NSP 15 plays an important role in mediating the evasion of host dsRNA sensors.[25]

Bioinformatics is an interdisciplinary branch of science which utilizes statistics, computer and mathematics to analyse biological data.[26] Bioinformatics is now used 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.[27] Docking analysis can be conducted for a particular 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.[28]

The aim of our study is to compare the best docking fit for the selected *Coriandrum sativum* L herbs constituents with the Dengue and MERS coronavirus proteins.

2. MATERIALS AND METHODOLOGIES

2.1. Preparation of viral proteins

The protein data bank (PDB) was used to obtain the three-dimensional image 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 in PDB format. Proteins of dengue and MERS coronavirus were used for this study. The 3D structure of all the thirteen proteins were downloaded from PDB and saved in PDB format. The downloaded proteins were viewed in Rasmol viewer.[29]

2.2. Preparation of ligands

Ligands selected were from the previous studies on GCMS analysis on *Coriandrum sativum* L herb extract.[8] 4 ligands were used for the study. Ligands were constructed using Chem Sketch.[30] 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 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.[31] The proteins and the ligands were loaded and the out path was set as desired. The Standard docking parameters used for docking the ligands with the Dengue and MERS coronavirus protein used was - (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 output path of 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 Rasmol viewer.[32]

3. RESULTS

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

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

Ligand	Compound name	Dengue Virus					MERS coronavirus			
		NS1 protein	Trans membrane domain of NS2A	NS2B / NS3 protease	NS3 helicase	NS5 protein	NSP 3	NSP 5	NSP 13	NSP 15
A	Dodecanal	-72.2	-527.7	-83.5	-80.3	-66.3	-69.0	-75.2	-69.7	-68.13
B	E-2-Dodecanol	-76.7	-568.4	-66.9	-77.6	-65.0	-65.2	-72.6	-65.7	-73.91
C	Decanal	-68.9	-431.1	-63.9	-66.5	-64.7	-73.5	-74.4	-65.8	-72.42
D	E-2-Decenol	-72	-510.6	-59.9	-68.9	-63.3	-66.4	-73.1	-61.0	-77.18

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

Ligand	Compound name	Dengue virus		MERS coronavirus	
		Capsid protein	Envelope protein	Spike glycoprotein	Nucleocaspid protein
A	Dodecanal	-69.1	-69.8	-61.3	-68.3
B	E-2-Dodecanol	-78.9	-64.9	-70.2	-70.9
C	Decanal	-65.6	-59.9	-72.3	-68.3
D	E-2-Decenol	-74.0	-58.9	-62.3	-63.9

3.2. H – Bond profile for Dengue and MERS coronavirus protein with 4 ligands.

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

Ligand	Compound name	Dengue Virus					MERS coronavirus			
		NS1 protein	Trans membrane Domain of NS2A	NS2B / NS3 protease	NS3 helicase	NS5 protein	NSP 3	NSP 5	NSP 13	NSP 15
A	Dodecanal	H-M	-	H-M	H-M H-S	-	H-M H-S	H-S	H-S	H-M
B	E-2-Dodecanol	H-M H-S	H-M H-S	H-S	H-M H-S	H-M	H-M H-S	H-M H-S	H-M H-S	H-M
C	Decanal	H-M	-	H-M H-S	-	H-M H-S	H-S	H-S	H-S	H-S
D	E-2-Decenol	H-M H-S	H-M	H-S	H-M	H-M	H-M	-	H-S	H-S

Table 4: H – bond profile for Dengue and MERS coronavirus structural proteins with 4 ligands.

Ligand	Compound name	Dengue virus		MERS coronavirus	
		Capsid protein	Envelope protein	Spike glycoprotein	Nucleocaspid protein
A	Dodecanal	H-M H-S	H-M	H-S	H-M
B	E-2-Dodecanol	H-M	H-M	H-S	H-M
C	Decanal	H-S	H-M	H-S	H-S
D	E-2-Decenol	H-S	H-M H-S	H-M H-S	H-M

3.3. Amino acid position profile for Dengue and MERS coronavirus protein with 4 ligands.

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

Ligand	Compound Name	Dengue Virus					MERS coronavirus			
		NS1 protein	Trans membrane Domain of NS2A	NS2B / NS3 protease	NS3 helicase	NS5 protein	NSP 3	NSP 5	NSP 13	NSP 15
A	Dodecanal	Ile (242)	-	Val (146)	Arg (463) Asn (464)	-	Val(11) Asp(12)	Ser (116)	Asn(107)	Asp(185)
B	E-2-Dodecanol	Asn (255)	Gly (3)	Asn (152)	Ser (321)	Thr (50)	Ala(184)	His (166)	Arg(161)	Ser(196)
C	Decanal	Cys (223)	-	Arg (55)	-	Ap (808)	Ser(146)	His (64)	Arg(139)	Asp(87)
D	E-2-Decenol	Asn (255)	Phe(15)	Arg (24)	Arg (463)	Ile (251)	Tyr(113)	-	Asn(381)	Asp(87)

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

Ligand	Compound name	Dengue virus		MERS coronavirus	
		Capsid protein	Envelope protein	Spike glycoprotein	Nucleocaspid protein
A	Dodecanal	Arg(22) Val(23) Ser(24)	Gly(628) Arg(629) Ile(630)	His(1146)	Gly(60)
B	E-2-Dodecanol	Ala(77)	Ile(616)	Arg(335)	Ala(75)
C	Decanal	Arg(68)	Ser(577)	Arg(141)	Thr(56)
D	E-2-Decenol	Arg(32)	Glu(638)	Asn(981)	Val(63)

4. DISCUSSION

Considering all the tables from Table – 1, to Table - 6, the 3D structure coordinates of seven proteins of dengue and six proteins of MERS coronavirus are optimized and 4 compounds

from *Coriandrum sativum* L herb extract were 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 MERS coronavirus 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 MERS coronavirus proteins are analyzed and the one having lowest ligand binding energy with these proteins among the different poses are generated. The lower total binding energy scores represent better protein-ligand target binding affinities as compared to higher total binding energy scores. Considering the structural proteins of Dengue virus, among the 4 analogs, compound "A " is found to have lower ligand binding energy (binding energy value = -69.8 kcal/mol), than other analogs for Envelope protein. Compound "B" has least binding energy score with Capsid protein (binding energy value = - 78.9 kcal/mol), the structural proteins of MERS coronavirus had following binding energies, Spike glycoprotein ('C' binding energy value = -72.3 kcal/mol), Nucleocapsid ('B', binding energy value = -70.9 kcal/mol)) The non structural proteins of Dengue virus had these binding energy values: Trans membrane domain of NS2A ('B', binding energy value = -568.4 kcal/mol), NS2B / NS3 protease ('A', binding energy value= -83.5 kcal/mol), NS3 helicase ('A', binding energy value = -80.3 kcal/mol), NS5 protein ('A', binding energy value = -66.3 kcal/mol) and NS1 protein ('B', binding energy value = -76.7 kcal/mol). And the non structural proteins of MERS coronavirus have, NSP 3 ('C', binding energy value = -73.5 kcal/mol), NSP 5 ('A', binding energy value = -75.2 kcal/mol), NSP 13('A', binding energy values = -69.7 kcal/mol) and NSP 15('D', binding energy value = -77.18 kcal/mol). We further analyzed the docked pose for finding the binding mode of compound "A" in to seven dengue and six MERS coronavirus 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 – B has best binding affinity with the target NS1 protein with the binding energy value of -76.7 kcal/mol . Interaction analysis of binding mode of compound –A in dengue virus NS1 protein reveals that it forms two hydrogen bonds with low energy, with Ile (243), Gly (249) and Asn

(255) residues. 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.

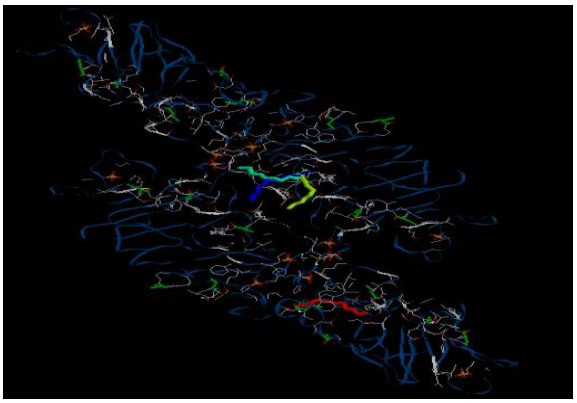

Fig. 1: The Total Binding Energy for Dengue virus NS1 protein with 4 ligands.

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 membrane domain of NS2A. From the docking study, we observed that compound – B has best binding affinity with the target Trans membrane domain of NS2A with the binding energy value of -568.4 kcal/mol. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus Trans membrane domain of NS2A reveals that it forms two hydrogen bonds with low energy, with Gly (3) residue with 4 ligands: is shown in Fig.2.

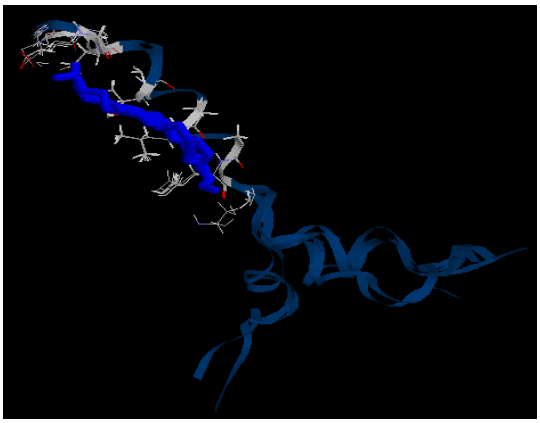

Fig. 2: The Total Binding Energy for Dengue virus Trans membrane domain of NS2A with 4 ligands.

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 / NS3 protease. From the docking study, we observed that compound – A has best binding affinity with the target NS2B / NS3 protease with the binding energy value of -83.5 kcal/mol. Interaction analysis of binding mode of compound –A in dengue virus NS2B / NS3 protease reveals that it forms one hydrogen bond with low energy, with Val(146) 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.

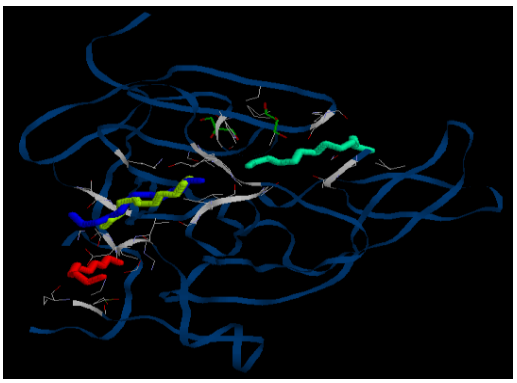

Fig. 3: The Total Binding Energy for Dengue virus NS2B / NS3 protease with 4 ligands.

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 NS3 helicase. From the docking study, we observed that compound – A has best binding affinity with the target NS3 helicase with the binding energy value of -80.3 kcal/mol. Interaction analysis of binding mode of compound –A in dengue virus NS3 helicase reveals that it forms two hydrogen bonds with low energy, with Arg (463) and Asn(464) residues. 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.

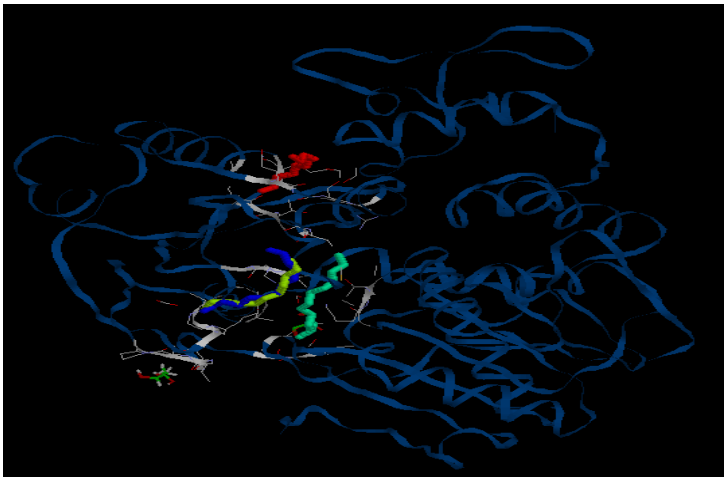

Fig. 4: The Total Binding Energy for Dengue virus NS3 helicase with 4 ligands.

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 – A has best binding affinity with the target NS5 protein with the binding energy value of -66.3 kcal/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.

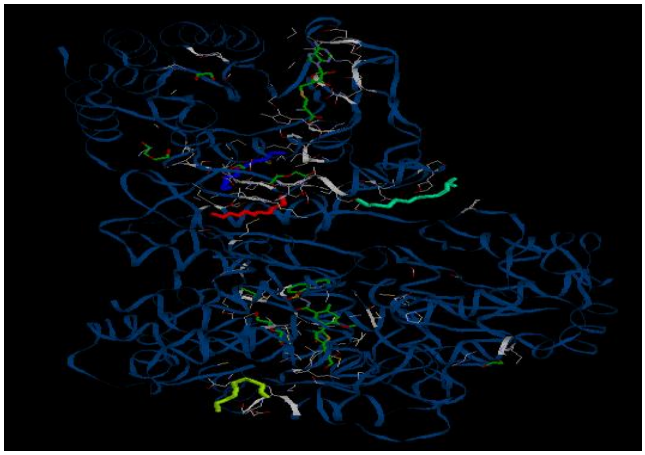

Fig. 5: The Total Binding Energy for Dengue virus NS5 protein with 4 ligands.

4.2. Non-Structural proteins of MERS coronavirus

4.2.1. The Total Binding Energy for MERS coronavirus NSP 3 protein with 4 ligands

From Table – 1, Table – 3 and Table – 5, the docking simulation of 4 ligands were performed for MERS coronavirus NSP 3 protein. From the docking study, we observed that compounds -C has best binding affinity with the target NSP 3 protein with the binding energy values of -73.5 kcal/mol. Interaction analysis of binding mode of compounds –C in dengue virus NSP 3

protein reveals that it forms one hydrogen bond with low energy, with Ser(146) residues. A close-up view of the Total Binding Energy (kcal/mol) profile for MERS coronavirus NSP 3 protein with 4 ligands: is shown in Fig.6.

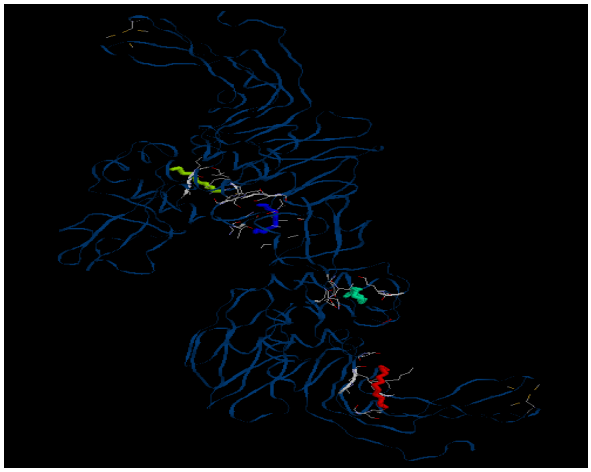

Fig. 6: The Total Binding Energy for MERS coronavirus NSP 3 protein with 4 ligands.

4.2.2. The Total Binding Energy for MERS coronavirus NSP 5 protein with 4 ligands:

From Table – 1, Table – 3 and Table – 5, the docking simulation of 4 ligands were performed for MERS coronavirus NSP 5 protein**.** From the docking study, we observed that compound – A has best binding affinity with the target NSP 5 protein with the binding energy value of -75.2 kcal/mol. Interaction analysis of binding mode of compound –A in dengue virus. NSP 5 protein reveals that it forms one hydrogen bond with low energy, with Ser (116) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for MERS coronavirus NSP 5 protein with 4 ligands: is shown in Fig.7.

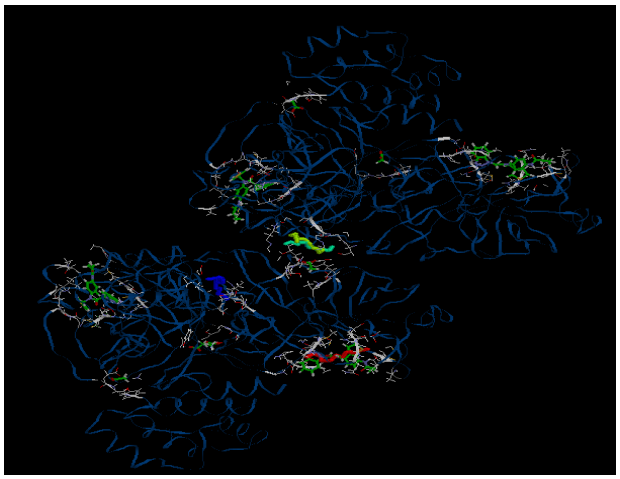

Fig. 7: The Total Binding Energy for MERS coronavirus NSP 5 protein with 4 ligands.

4.2.3. The Total Binding Energy for MERS coronavirus NSP 13 protein with 4 ligands:

From Table – 1, Table – 3 and Table – 5, the docking simulation of 4 ligands were performed for MERS coronavirus NSP 13 protein. From the docking study, we observed that compound – A has best binding affinity with the target NSP 13 protein with the binding energy value of -69.7 kcal/mol. Interaction analysis of binding mode of compound –A in dengue virus. NSP 13 protein reveals that it forms one hydrogen bond with low energy, with Asn (107) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for MERS coronavirus NSP 13 protein with 4 ligands: is shown in Fig.8.

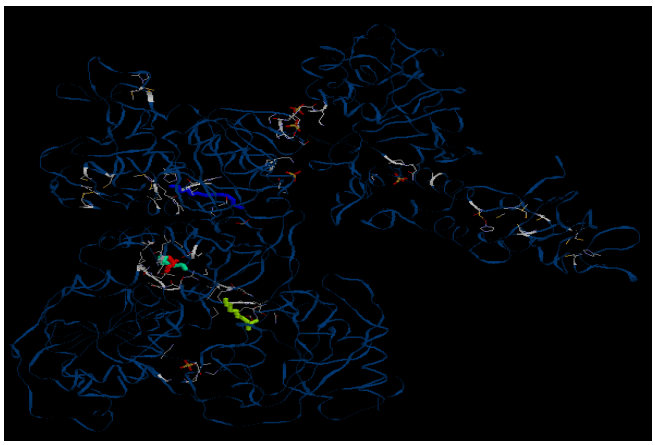

Fig. 8: The Total Binding Energy for MERS coronavirus NSP 13 protein with 4 ligands.

4.2.4. The Total Binding Energy for MERS coronavirus NSP 15 protein with 4 ligands

From Table – 1, Table – 3 and Table – 5, the docking simulation of 4 ligands were performed for MERS coronavirus NSP 15 protein. From the docking study, we observed that compound – D has best binding affinity with the target NSP 15 protein with the binding energy value of -77.18 kcal/mol. Interaction analysis of binding mode of compound –D in dengue virus. NSP 15 protein reveals that it forms one hydrogen bond with low energy, with Asp(87) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for MERS coronavirus NSP 15 protein with 4 ligands: is shown in Fig.9.

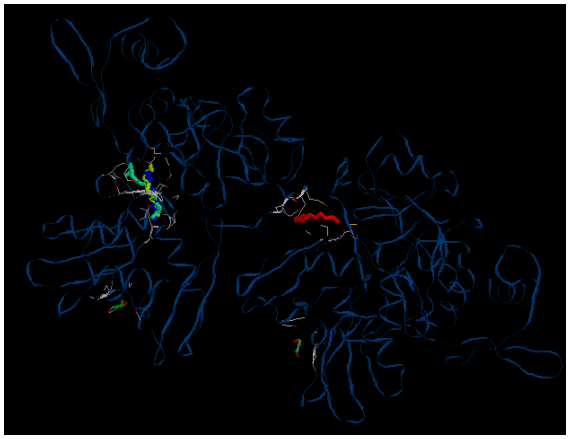

Fig. 9: The Total Binding Energy for MERS coronavirus NSP 15 protein with 4 ligands.

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 – B has best binding affinity with the target Capsid protein with the binding energy value of -78.9 kcal/mol. Interaction analysis of binding mode of compound –B in dengue virus. Capsid protein reveals that it forms one hydrogen bond with low energy, with Ala(77) 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.

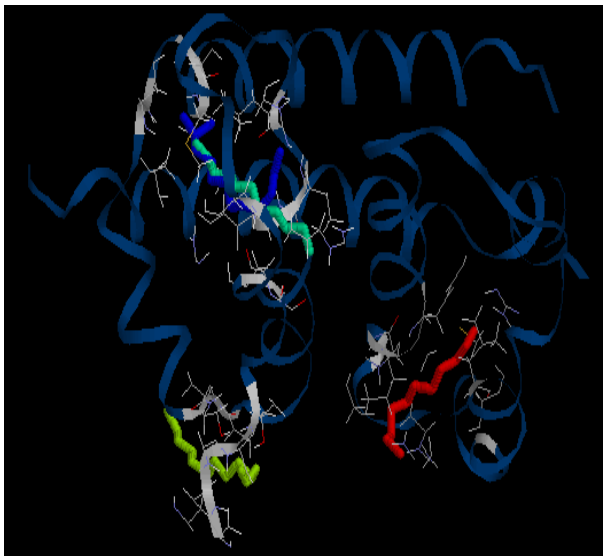

Fig. 10: The Total Binding Energy for Dengue virus Capsid protein with 4 ligands.

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 – A has best binding affinity with the target envelope protein with the binding energy value of -69.8 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 Gly (628), Arg (629) and Ile (630) residues. 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.

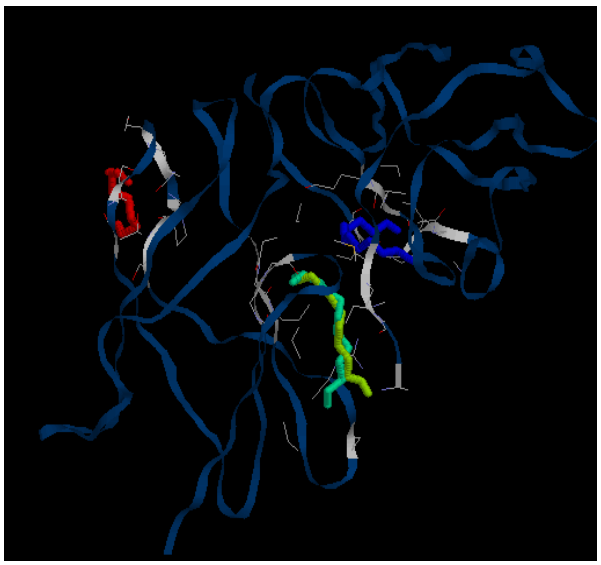

Fig. 11: The Total Binding Energy for Dengue virus envelope protein with 4 ligands.

4.4. Structural proteins of MERS coronavirus

4.4.1. The Total Binding Energy for MERS coronavirus Spike glycoprotein with 4 ligands

From Table – 2, Table – 4 and Table – 6, the docking simulation of 4 ligands were performed for MERS coronavirus Spike glycoprotein. From the docking study, we observed that compound – C has best binding affinity with the target Spike glycoprotein with the binding energy value of -72.3 kcal/mol. Interaction analysis of binding mode of compound –C in dengue virus Spike glycoprotein reveals that it forms one hydrogen bond with low energy, with Arg (141) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for MERS coronavirus Spike glycoprotein with 4 ligands: is shown in Fig.12.

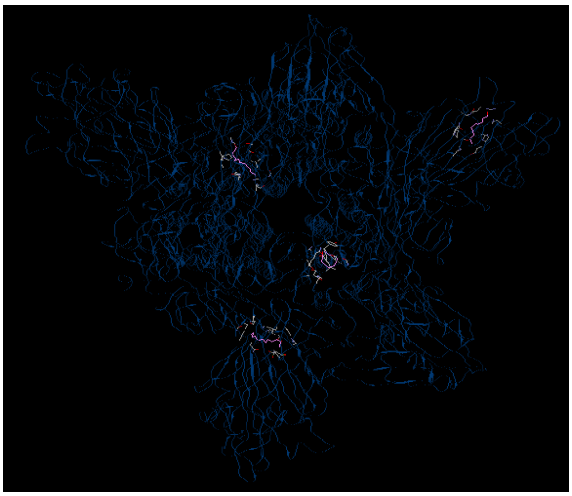

Fig. 12: The Total Binding Energy for MERS coronavirus Spike glycoprotein with 4 ligands.

4.4.2. The Total Binding Energy for MERS coronavirus Nucleocapsid protein with 4 ligands

From Table – 2, Table – 4 and Table – 6, the docking simulation of 4 ligands were performed for MERS coronavirus Nucleocaspid protein. From the docking study, we observed that compound – B has best binding affinity with the target Nucleocaspid protein with the binding energy value of -70.9 kcal/mol. Interaction analysis of binding mode of compound –B in dengue virus Nucleocaspid protein reveals that it forms one hydrogen bond with low energy, with Ala(75) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for MERS coronavirus Nucleocaspid protein with 4 ligands: is shown in Fig.13.

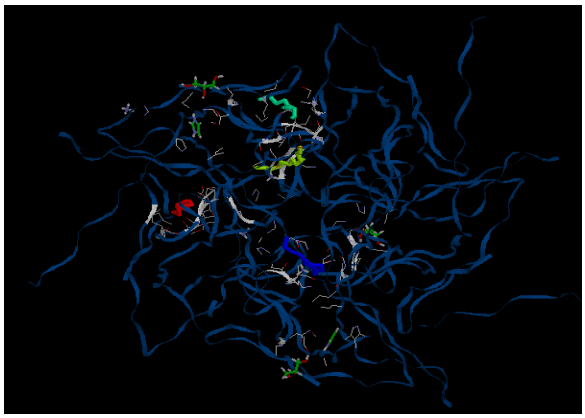

Fig. 13: The Total Binding Energy for MERS coronavirus Nucleocapsid protein with 4 ligands.

5. CONCLUSION

Our molecular docking studies explored the possible binding modes of 4 compounds that are present in *Coriandrum sativum* L herb with seven proteins of Dengue virus and six proteins of MERS coronavirus. Dengue virus consists of envelope protein, NS1 protein, Transmembrane doamin of NS2A, NS2B/NS3 protease, NS3 helicase, NS5 protein and capsid protein; MERS coronavirus consists of Spike glycoprotein, Nucleocapsid protein, NSP 3 protein, NSP 5 protein, NSP 13 protein and NSP 15 protein. It revealed that all the 4 compounds show minimum affinity with all the proteins. The compound A (Dodecanal) 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 B has highest binding affinity with most of the structural proteins of Dengue virus as well as with the majority of the structural proteins of MERS coronavirus. Whereas the compound A is shown to have highest binding affinity with most of the non structural proteins of Dengue virus and the non structural proteins of MERS coronavirus has highest binding affinities with both A and B compounds and therefore it can be used as an effective drug target for Dengue virus as well as MERS coronavirus . Hence, the Compound C may be considered as the effective drug target for both dengue and MERS coronavirus 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 throw light for the future development of more potent drugs for the treating of Dengue and MERS.

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