WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 7, Issue 19, 1290-1304. Research Article ISSN 2277– 7105

IN SILICO STUDIES ON DENGUE AND MARBURG VIRAL PROTEINS WITH SELECTED *MURRAYA KOENIGII* LEAVES CONSTITUENTS

[1]Rameen Taj S., [1]Sheetal V. Rao, [1]Tulasi D. P., [1]Nisha R., [1]Pavithra K. 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.

Article Received on
15 October 2018,
Revised on 05 Nov. 2018,
Accepted on 25 Nov. 2018
DOI: 10.20959/wjpr201819-13825

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

ABSTRACT

Dengue and Marburg virus contains seven and six proteins respectively, 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 Marburg disease in humans. Phytochemicals present in *Murraya koenigii* can be used to prevent premature graying of hair and kidney pain. It has got antibacterial activity, anti fungal activity, anti protozoal activity. In this particular study, the binding efficiency of 5 compounds present in the *Murraya koenigii* with all the thirteen viral proteins was performed through in silico methods. By our molecular docking result, we found that the 2-Phenyl-4 Quinolinecarboxamide have highest binding affinity with the proteins and we also predicted the binding site amino acid residues and the type of hydrogen bonding.

KEYWORDS: *Murraya koenigii*, molecular docking, binding affinities, 2-Phenyl-4 Quinolinecarboxamide.

1. INTRODUCTION

Medicinal plants and their bioactive compounds have been utilised for primary and traditional health care system since time immemorial.[1] They are the "backbone" of traditional medicine, which means more than 3.3 billion people in the less developed countries utilize

medicinal plants on a regular basis. These medicinal plants considered as a rich resource of ingredients which can be used in drug development and synthesis. These plants play a critical role in the development of human cultures. *Murraya Koenigii* (Rutaceae) commonly known as Meethi neem, is an aromatic more or less deciduous shrub or a small tree up to 6m in height.[2] Curry leaf (*Murraya Koenigii*) is an important leafy vegetable. Its leaves are widely used in Indian cookery for flavouring food stuffs. Thus, the curry leaf is also used in many of the Indian Ayurvedic and Unani Prescriptions. Curry leaves are a popular leaf spice used in very small quantities for their distinct aroma due to the presence of volatile oil and their ability to improve digestion.[3] Apart from *Murraya Koenigii* that also shows some antifungal, anti-oxidative, cytotoxic, antimicrobial, antibacterial, antiulcer, anti diarrhoeal, dysentery, febrifuge, blood purifier, tonic, stomachic, positive ionotropic and cholesterol reducing properties.[2,3]

GC-MS chromatogram of the methanolic extract of *Murraya Koenigii* showed five major peaks, GC-MS analysis revealed the presence of α.-Caryophyllene, 2-phenyl-4-quinolinecarboxamide, Phenanthrene, 10H-Phenoxaphosphine, 1,5-Diformyl-2,6-Dimethoxy-Anthracene. Keeping in view the tremendous pharmacological activities of its constituents and *Murraya koenigii* may be utilized to alleviate the symptoms of variety of diseases. Although the extracts of various parts of M. koenigii has numerous medical applications indifferent disorders, modern drugs can be developed based on its bioactivity, pharmaco-therapeutics, and mechanism of action, toxicity and after proper standardization. The wide spread of availability and extensive literature of M. koenigii in India thus makes it an attractive target for further pre-clinical and clinical research.[1]

Dengue virus (DV), an arthoropod-borne flavivirus, cause a febrile illness for which their is no antiviral treatment and no vaccine.[4] The origin of word is derived from Swahili Phrase ka-dinga pepo from Spanish. The word dengue, meaning fastidious or careful. It is second disease after “yellow fever” that was shown to be caused by virus. Dengue hemorrhagic fever is first reported in Phillippines.[5] Dengue virus is a positive-stranded encapsulated RNA virus. The genomic RNA is approximately 11kb in length and is composed of three structural proteins genes that encode the encode the nucleocapsid, a membrane-assoicated protein, envelope protein and seven non-structural proteins genes.[6] The seven non structural proteins have identified they are capsid protein, envelope protein, NS1 protein, trans membrane domain of NS2A, NS2B/NS3 protease, NS3 helicase and NS5 protein. NS2B-NS3 protease is

a crucial enzyme for the viral replication.[7] NS2B/ NS3 protease has an important role in the viral life cycle.[8] A structural protein called envelop protein is involved in the viral assembly. The capsid protein is one of the structural proteins, which is involved in the encapsidation of the viral genome.[9] 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.[10] NS3 helicase belongs to the non-structural and a multi-domain dengue virus replication protein.[11] 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 is involved in the replication of the viral genome. RNA is synthesized via "de novo" by NS5 protein.[12]

Marburg (MBG), Ebola and Reston viruses are the members of the Filoviridae, the third family of negative- strand RNA viruses with non-segmented genomes (Order Mononegavirales) besides the Paramyxoviridae and Rhabdoviridae. The mortality rate of MBG infection was unusually high: 30% of the cases had a fatal outcome. MBG is a bacillus-shaped virus (680 nm in length and 80 nm in diameter) composed of seven structural proteins.[13] The genome of the Marburg virus is 11 kb long, which has six open reading frames encoding structural proteins, including the virion envelope glycoprotein (GP), nucleoprotein (NP), matrix proteins VP40, transcriptional factor VP30, nucleocapsid VP35 and VP24. VP24 protein has effective role in inhibiting the host IFN response[14] VP35 is a suppressor of RNA silencing and important for viral invasion of the innate immune response.[15] VP30 has the primary role of initiating EBOV transcription.[16]

Bioinformatics is the application of computational tools to organize, analyze, understand, visualize and store information associated with biological macromolecule.[17] 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.[18] 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.[19]

The aim of our study is to compare the best docking fit for the selected *Murraya Koenigii* leaves constituents with the Dengue and Marburg viral proteins.

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 Marburg 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.[20]

2.2. Preparation of ligands

Ligands selected were from the previous studies on GCMS analysis on *Murraya koenigii* leaves extract.[21] 5 ligands were used for the study. Ligands were constructed using Chem Sketch.[22] 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,D and E 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.[23] 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.[24]

3. RESULTS

3.1. Total Binding Energy (kcal/mol) profile for Dengue and Marburg viruses proteins with 5 ligands.

Table 1: The Total Binding Energy (kcal/mol) profile for Dengue and Marburg viruses structural proteins with 5 ligands.

Ligand	Compound name	Dengue Virus		Marburg virus					
		Capsid protein (1R6R)	Envelop protein (3WE1)	Nucleoprotein (5F5M)	Matrix Protein (VP40)	Glycoprotein	VP 35	VP 24	Transcription Factor(VP30)
A	1,5 Diformyl-2,6 dimethoxy-ant	-81.2	-94.2	-96.5	-96.9	-87.4	-73.4	-99.9	-94.0
B	2-Phenyl-4 Quinolinecarboxamide	-81.5	-80.3	-88.2	-102.8	-75.0	-74.6	-107.5	-90.8
C	10-H Phenoxaphosphinine	-76.4	-67.9	-67.6	-70.0	-70.3	-60.7	-75.1	-72.0
D	Alpha caryophyllene	-60.2	-60.3	-65.2	-64.0	-55.2	-51.1	-74.4	-66.5
E	Phenanthrene	-78.3	-62.8	-75.9	-72.1	-74.5	-58.3	-77.6	-75.2

3.2. H – Bond profile for Dengue and Marburg viruses protein with 5 ligands.

Table 2: H – bond profile for Dengue and Marburg viruses structural proteins with 5 ligands.

Ligand	Compound name	Dengue virus		Marburg virus					
		Capsid protein	Envelope protein	Nucleoprotein	VP40- Matrix protein	Glycoprotein	VP 35	VP 24	Transcription Factor(VP30)
A	1,5 Diformyl-2,6 dimethoxy-ant	H-S	H-M	H-M	H-S	H-S	H-S	H-S	H-M
B	2-Phenyl-4 Quinolinecarboxamide	H-S	H-M	H-M	H-S	H-S	H-M	H-M	H–S H-M
C	10-H Phenoxaphosphinine	-	H-M	H-M	-	-	-	-	-
D	Alpha caryophyllene	-	-	-	-	-	-	-	-
E	Phenanthrene	-	-	-	-	-	-	-	-

3.3. Amino acid position profile for Dengue and Marburg viruses protein with 5 ligands.

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

Ligand	Compound name	Dengue virus		Marburg virus					
		Capsid protein	Envelope protein	Nucleoprotein	VP40- Matrix protein	Glycoprotein	VP 35	VP 24	Transcription Factor(VP30)
A	1,5 Diformyl-2,6 dimethoxy-ant	Arg (32)	Ile (630)	Ala (300)	Arg (139)	Arg (560)	Arg (258)	His (168)	Tyr (139)
B	2-Phenyl-4 Quinolinecarboxamide	Thr (62)	Ser (633) Leu (636)	Gly (225) Leu (290) His (292)	Gln (143)	Arg (560)	Pro (304) Pro(305)	Val (35)	Lys (187) Asn (189) Arg (186)
C	10-H Phenoxaphosphinine	-	Arg (629) Ile (630)	Ser (121)	-	-	-	-	-
D	Alpha caryophyllene	-	-	-	-	-	-	-	-
E	Phenanthrene	-	-	-	-	-	-	-	-

4. DISCUSSION

Considering all the tables from Table – 1, Table – 2 and Table - 3, the 3D structure coordinates of two non proteins of dengue and six proteins of Marburg viruses are optimized and 5 compounds from *Murraya Koenigii* leaves extract are identified. The total binding energy of the compounds with all the eight proteins was calculated using iGEMDOCK. Evaluations of binding conformation of these 5 compounds with two dengue as well as Marburg viral proteins are performed using iGEMDOCK. From docking study, we listed binding affinities of 5 compounds based on ligand binding energy (Table- 1). The binding pose for each ligand molecule into the dengue and Marburg 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 5 analogs, compound “D” is found to have lower ligand binding energy (binding energy

value= -60.2 kcal/mol), than other analogs for Envelope protein. Compound "D" has least binding energy score with caspid protein (binding energy value= -60.3kcal/mol), the structural proteins of marburg virus had following binding energies, Nucleoprotein('A' binding energy value= -96.5 kcal/mol), VP40 Matrix protein('B' binding energy value= -102.8 kcal/mol), VP24('B', binding energy value= -107.5 kcal/mol), Glycoprotein('A', binding energy value= -87.4 kcal/mol), VP30 ('A', binding energy value= -94 kcal/mol) and VP35 ("B", binding energy value= -74.6 kcal/mol). We further analyzed the docked pose for finding the binding mode of compound "A" and compound "C" in to two dengue and six Marburg viral proteins to validate the reasonable binding conformations.

4.1. Structural proteins of Dengue virus

4.1.1. The Total Binding Energy for Dengue virus Capsid protein with 5 ligands

From Table – 1, Table – 2 and Table – 3, the docking simulation of 5 ligands were performed for Dengue virus Capsid protein. From the docking study, we observed that compound – D has best binding affinity with the target Capsid protein with the binding energy value of -60.3kcal/mol. Interaction analysis of binding mode of compound –D in dengue virus Capsid protein reveals that it forms no hydrogen bond with low energy. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus Capsid protein with 5 ligands: is shown in Fig.1.

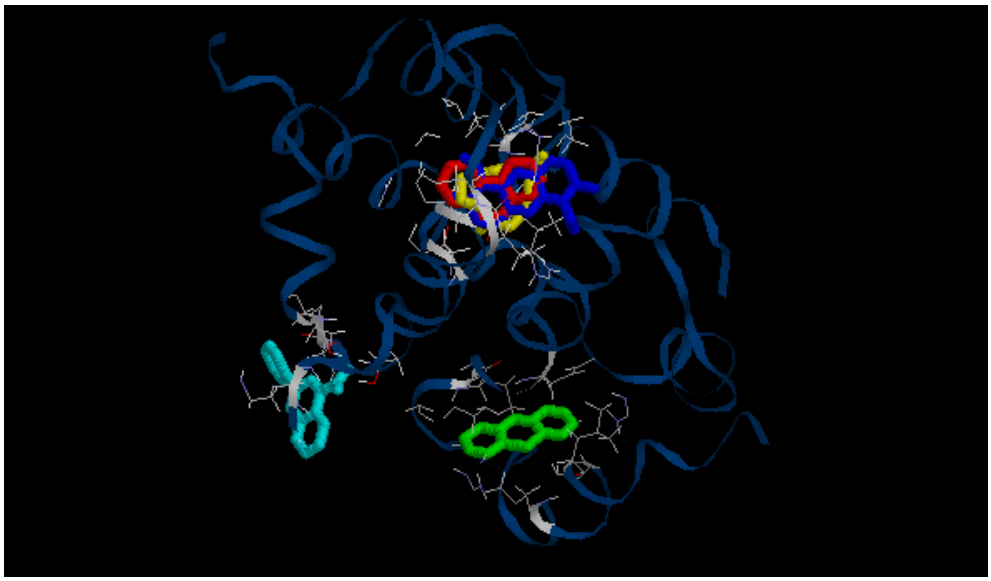

Fig. 1: The Total Binding Energy for Dengue virus Capsid protein with 5 ligands.

4.1.2. The Total Binding Energy for Dengue virus envelope protein with 5 ligands

From Table – 1, Table – 2 and Table – 3, the docking simulation of 5 ligands were performed for Dengue virus envelope protein. From the docking study, we observed that compound – D has best binding affinity with the target envelope protein with the binding energy value of -60.2kcal/mol. Interaction analysis of binding mode of compound –D in dengue virus envelope protein reveals that it forms no hydrogen bond with low energy. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus envelope protein with 5 ligands: is shown in Fig.2.

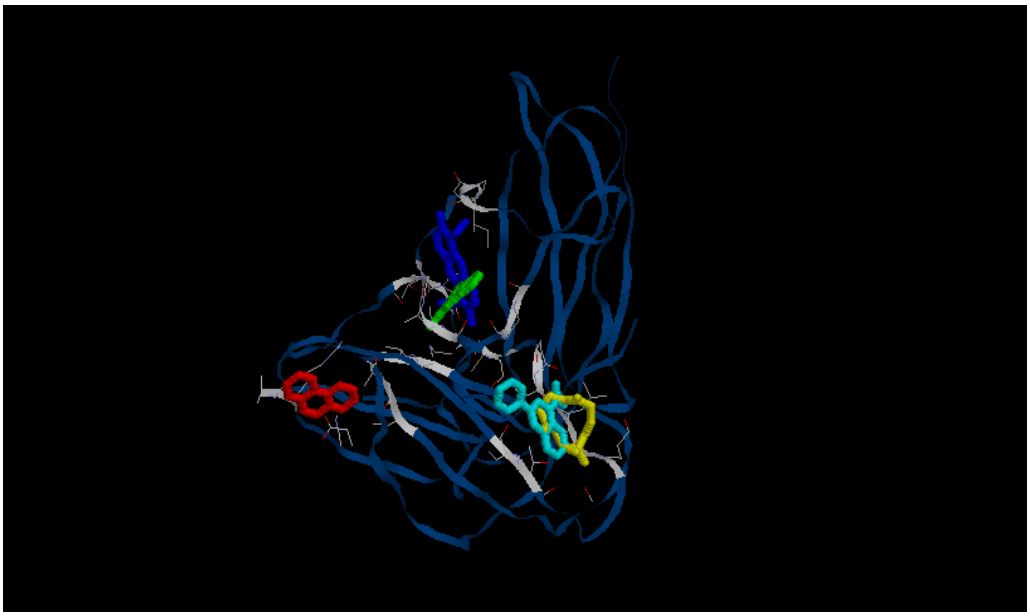

Fig. 2: The Total Binding Energy for Dengue virus envelope protein with 5 ligands

4.2. Structural proteins of Marburg virus

4.2.1. The Total Binding Energy for Marburg virus Nucleoprotein protein with 5 ligands.

From Table – 1, Table – 2 and Table – 3, the docking simulation of 5 ligands were performed for Marburg virus Nucleoprotein. From the docking study, we observed that compound – A has best binding affinity with the target Nucleoprotein with the binding energy value of -96.5kcal/mol. Interaction analysis of binding mode of compound –A in dengue virus Nucleoprotein reveals that it forms one hydrogen bond with low energy, with Ala (300) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Marburg virus Nucleoprotein with 5 ligands: is shown in Fig.3.

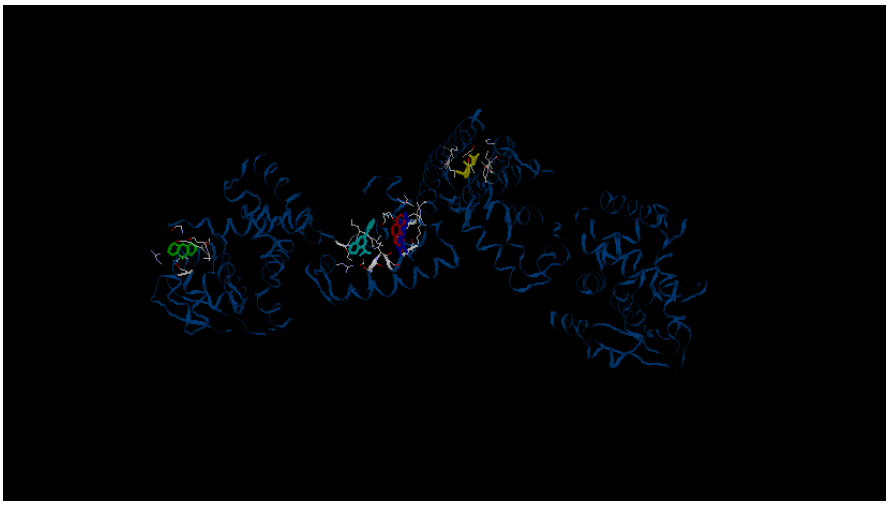

Fig. 3: The Total Binding Energy for Marburg virus nucleoprotein with 5 ligands.

4.2.2. The Total Binding Energy for Marburg virus VP40 Matrix protein with 5 ligands

From Table – 1, Table – 2 and Table – 3, the docking simulation of 5 ligands were performed for Marburg virus VP40 Matrix protein. From the docking study, we observed that compound – B has best binding affinity with the target VP40 Matrix protein with the binding energy value of -102.8kcal/mol. Interaction analysis of binding mode of compound –B in dengue virus VP40 Matrix protein reveals that it forms one hydrogen bonds with low energy, with Gln (143) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Marburg virus VP40 Matrix protein with 5 ligands: is shown in Fig.4.

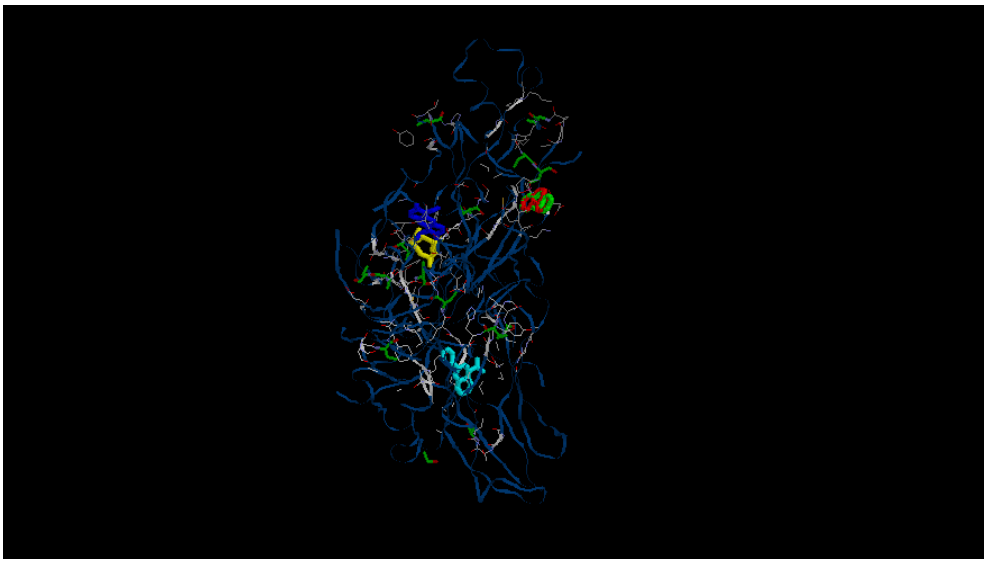

Fig. 4: The Total Binding Energy for Marburg virus VP40 Matrix protein with 5 ligands.

4.2.3. The Total Binding Energy for Marburg virus VP24 Nucleocaspid protein with 5 ligands:

From Table – 1, Table – 2 and Table – 3, the docking simulation of 5 ligands were performed for Marburg virus VP24 Nucleocaspid protein. From the docking study, we observed that compound – B has best binding affinity with the target VP24 Nucleocaspid protein with the binding energy value of -107.5 kcal/mol. Interaction analysis of binding mode of compound – B in dengue virus VP24 Nucleocaspid protein reveals that it forms one hydrogen bond with low energy, with Val (35) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Marburg virus VP24 Nucleocaspid protein with 5 ligands: is shown in Fig.5.

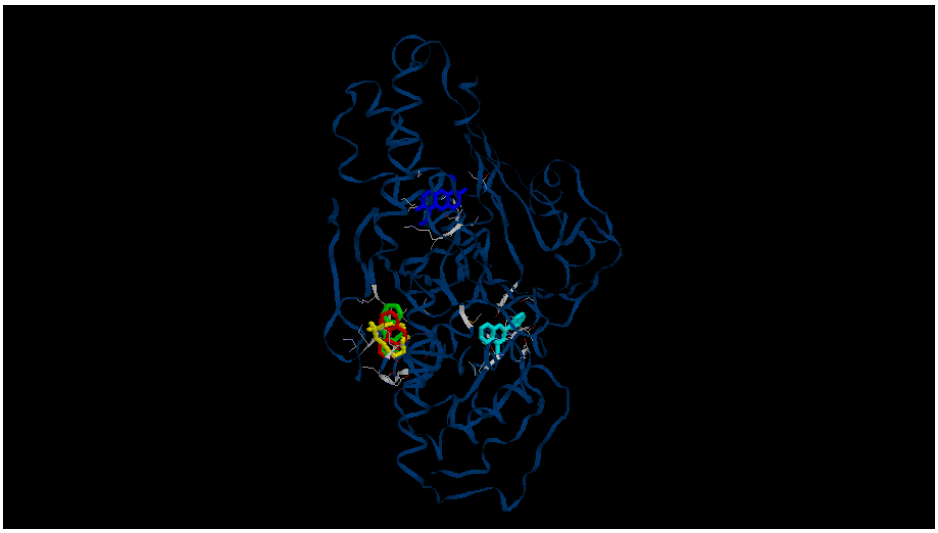

Fig. 5: The Total Binding Energy (kcal/mol) profile for Marburg virus VP24 Nucleocaspid protein with 5 ligands.

4.2.4. The Total Binding Energy for Marburg virus glycoprotein with 5 ligands

From Table – 1, Table – 2 and Table – 3, the docking simulation of 5 ligands were performed for Marburg virus gylcoprotein From the docking study, we observed that compound –A has best binding affinity with the target glycoprotein with the binding energy value of -87.4kcal/mol. Interaction analysis of binding mode of compound – A in dengue virus glycoprotein reveals that it forms one hydrogen bond with low energy, with Arg (560) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Marburg virus glycoprotein with 5 ligands: is shown in Fig.6.

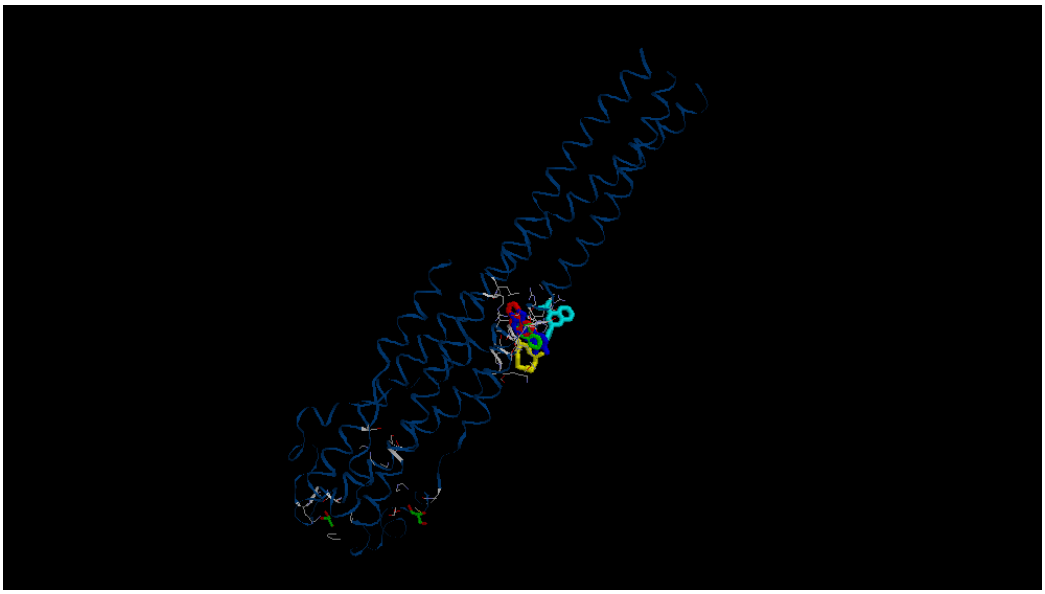

Fig. 6: The Total Binding Energy for Marburg virus glycoprotein protein with 5 ligands.

4.2.5. The Total Binding Energy for Marburg virus VP30 with 5 ligands.

From Table – 1, Table – 2 and Table – 3, the docking simulation of 5 ligands were performed for Marburg virus VP30 Transcription Fatctor. From the docking study, we observed that compound – A has best binding affinity with the target VP30 Transcription Fatctor with the binding energy value of -94 kcal/mol. Interaction analysis of binding mode of compound –A in dengue virus VP30 Transcription Fatctor reveals that it forms one hydrogen bond with low energy, with Tyr (139) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Marburg virus VP30 Transcription Factor with 5 ligands: is shown in Fig.7.

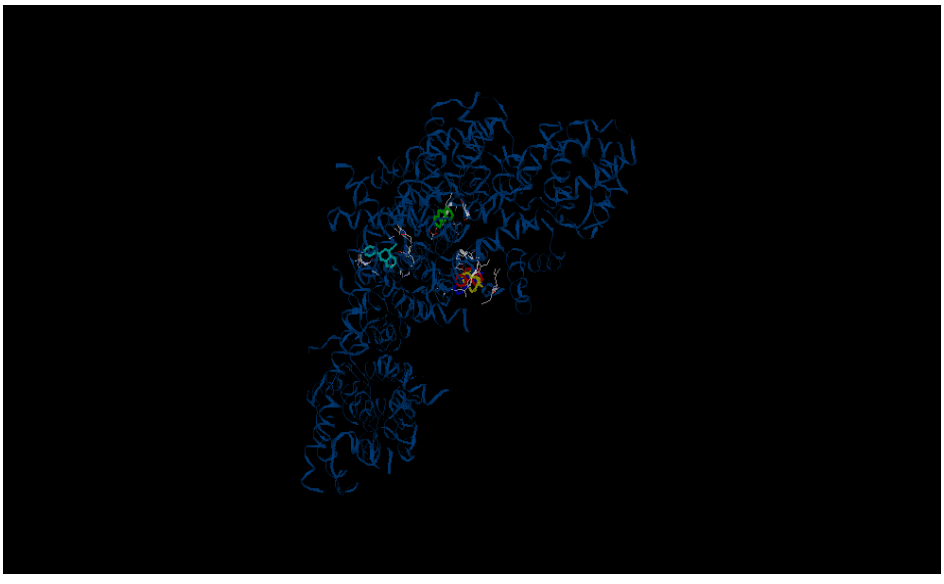

Fig. 7: The Total Binding Energy for Marburg virus VP30 with 5 ligands.

4.2.6. The Total Binding Energy for Marburg virus VP35 with 5 ligands

From Table – 1, Table – 2 and Table – 3, the docking simulation of 5 ligands were performed for Marburg virus VP35. From the docking study, we observed that compound – B has best binding affinity with the target VP35 with the binding energy value of -74.6 kcal/mol. Interaction analysis of binding mode of compound –B in dengue virus VP35 reveals that it forms one hydrogen bond with low energy, with Pro (304) and Pro (305) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Marburg virus VP35 with 5 ligands: is shown in Fig.8.

Fig.8: The Total Binding Energy for Marburg virus VP35 with 5 ligands.

5. CONCLUSION

Our molecular docking studies explored the possible binding modes of 5 compounds that are present in *Murraya Koenigii* leaf with two proteins of Dengue virus and six proteins of Marburg virus. Dengue virus consists of envelope protein and capsid protein; Marburg virus consists of Glycoprotein, Nucleoprotein, VP40 Matrix protein, VP24 Nucleocaspid protein, VP35, VP30. It revealed that all the 5 compounds show minimum affinity with all the proteins. The compound B (2-Phenyl-4 Quinolinecarboxamide) 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 and compound D has the highest binding affinity with majority of the structural proteins of Marburg virus therefore it can be used as an effective drug target for Dengue virus as well as Marburg virus. Hence, the Compound B may be considered as the effective drug target for

both dengue and Marburg 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 Marburg.

6. REFERENCES

1. Balasubramanian. S, Ganesh Dama, Surya Narayana VVS, P. Sreedhar Reddy, "GC-MS analysis of the Curry leaves (*Murraya koengii*)", *Global Journal of Biology, Agriculture and Health Sciences*, 2014; 3(2): 8–10.
2. Satish Chand Saini, Gopu Bala Show Reddy, "A review on Curry Leaves *(Mjurraya Koenigii)*: Versatile Multi-Potential Medicinal Plant", 2015; 3(4): 363–368.
3. Singh R. "Medicinal Plants: A Review". *Journal of Plant Sciences*, 2015; 3(1-1): 50–55.
4. Shuenn-Jue L. Wu, Geraldine Grouard-Vogel, Wellington Sun, John R, Mascola, Elena Brachetl, Ravithat Putvatnana, Mrak K. Louder, Luis Filgueria, Mary. A. Marvich, Henry K. Wong, Andrew Blauvelt, Gerald S. Murphy, Merlin L.Robb, Bruce L.Innes, Djeeorah L.Birx, Curtis G. Haves and Sarah Schlesinger Frankel, "Human skin Langerhans cells are targets of dengue virus infection", *Nat Med*, 2000; 6(7): 816-20.
5. Vaddadi Srinivas, Vaddadi Radha Srinivas, "Dengue Fever: A Review Article", *Journal of Evolution of Medical and Dental Sciences*, 2015; 4(29): 5048-5058.
6. Pei-Yun Shu and Jyh-Hsiung Huang, "Current Advances in Dengue Diagnosis", *Clin Diagn Lab Immunol*, 2004; 11(4): 642–650.
7. Prakash P, Gupta N. "Therapeutic uses of *Ocimum sanctum Linn* (Tulsi) with a note on eugenol and its pharmacological actions: a short review". *Indian J Physiol Pharmacol*, 2005; 49(2): 125-131.
8. Bhartiya US, Raut YS, Joseph LJ. "Protective effect of Ocimum sanctum L after high-dose 131iodine exposure in mice: an in vivo study". *Indian J Exp Biol*, 2006; 44(8): 647- 652.
9. Singh V Amdekar S and Verma O. "*Ocimum Sanctum* (tulsi): Bio-pharmacological Activities, *Web med Central. Pharmacol*, 2010; 1(10): WMC001046.

10. Balasubramanian S, Ganesh D, Shridhar Reddy P, Surya Narayana VVS. "GC-MS Analysis of Phytocomponents in the Methanolic Extract of *Ocimum Sanctum* (Tulsi)". *Asian Journal of Pharmaceutical Analysis and Medicinal Chemistry*, 2014; 2(2): 71–75.
11. Ab-Fatah M, Subenthiran S, Abdul-Rahman PSA, Saat Z, Thayan R; "Research Note Dengue Serotype Surveillance Among Patients Admitted for Dengue in Two Major Hospitals in Selangor, Malaysia. Kuala Lumpur'. *Tropical biomedicine*, 2015; 32(1): 187–191.
12. Mishra B, Sharma M, Pujhari SK, Ratho RK, Gopal DS, Kumar CN, Sarangi G, Chayani N, Varma SC; "Utility of Multiplex Reverse transcriptase - Polymerase Chain Reaction for Diagnosis and Serotypic Characterization of Dengue and Chikungunya Viruses in Clinical Samples". *Diagnostic microbiology and infectious disease*, 2011; 71(2): 118–125.
13. Parekh J, Chanda S; "Antibacterial and Phytochemical Studies on Twelve Species of Indian Medicinal Plants". *African Journal of Biomedical Research*, 2007; 10(2): 175-181.
14. Sarangi KM, Padhi S; "Dengue and its Phytotherapy A Review". *International Journal of Pharmaceutical and Phytopharmacological Research.* 2017; 4(1): 37–46.
15. Ma L, Jones CT, Groesch TD, Kuhn RJ Post CB; "Solution Structure of Dengue Virus Capsid Protein Reveals another Fold". *Proc. Natl. Acad. Sci*, 2004; 101: 3414–3419.
16. Xie X, Gayen S, Kang C, Yuan Z, Shi PY; "Membrane Topology and Function of Dengue VirusNS2A Protein". *J. Virol*, 2013; 87: 4609–4622.
17. Perera R, Kuhn RJ; "Structural Proteomics of Dengue Virus". *Curr Opin Microbiol*, 2008; 11; 4: 369–377.
18. Lim SP, Noble CG, Seh CC, Soh TS, El Sahili A, Chan GK, Lescar J, Arora R, BensonT, Nilar S, Manjunatha U, Wan KF, Dong H, Xie X, Shi PY, Yokokawa F. "Potent Allosteric Dengue Virus NS5 Polymerase Inhibitors: Mechanism of Action and Resistance Profiling". *PLoS Pathog*, 2016; 12(8): e1005737.
19. Stephean Becker, Martha Spiess and Hans-Dieter Klenk, "The asialogylcoprotein receptor is a potential liver-specific receptor for Marburg virus". *Journal of General Virology*, 1995; 76(Pt2): 393-399.
20. Reid S P, Leung LW, Hartman AL, Martinez O, Shaw ML, Carbonnelle. "*Ebola* virus VP24 binds karyopherin alpha1 and blocks STAT1 nuclear accumulation". *J Virol*, 2006; 80(11): 5156–5167.
21. Haasnoot J, De vries W, Geutijes EJ, Prins M, De Haan P, Berkhout B. "The ebola virus VP35 protein is a suppressor of RNA silencing", *PLoS Pathlog*, 2007; 3(6): e86.

22. Weik M, Modrof J, Klenk H-D, Becker S, Muhlberger E. " Ebola virus VP30 mediated transcription is regulated by RNA secondary structure formation. *J Virol*, 2002; 76(17): e86.
23. Smriti Chawla, Pavithra.K, Rituparna Chatterjee, Balasubramanian Suathyamurthy. "Docking Study Of Selected Red Vitis Vinifera Peel Constituents On Dengue Viral Proteins-An In Silico Approach". *Indo American Journal Of Pharmaceutical Sciences*, 2018; 05(11): 11818-11826.
24. Berman HM, Westbrook J, Feng Z, Gilliland G, Bhat TN, Weissig H, Shindyalov IN, Bourne PE. "The Protein Data Bank". *Nucleic Acids Research*, 2000; 28(1): 235–242.
25. Ferreira LG, Ricardo N, Oliva G, Andricopulo AD. "Molecular Docking and Structure-Based Drug Design Strategies". *Molecules*, 2015; 20: 13384–13421.
26. Sushmitha H. S, Balasubramanian Sathyamurthy. "In Silico drug designing studies on Dengue Virus NS2BNS3 Protease", *Indo American Journal of Pharmaceutical Sciences*. 2018; 5(8): 7784–7790.
27. Balasubramanian S, Ganesh D, Shridhar Reddy P, Surya Narayana VVS. "GC-MS Analysis of Phytocomponents in the Methanolic Extract of *Ocimum Sanctum* (Tulsi)". *Asian Journal of Pharmaceutical Analysis and Medicinal Chemistry*, 2014; 2(2): 71–75.
28. Sushmitha H. S, Balasubramanian Sathyamurthy. "In Silico drug designing studies on Dengue Virus Envelope Protein". *World Journal of Pharmaceutical sciences*, 2018; 6(9): 138–143.
29. Sushmitha H. S, Balasubramanian Sathyamurthy. "In Silico drug designing studies on Dengue Virus NS3 Helicase". *European Journal of Biomedical and Pharmaceutical sciences*, 2018; 5(9): 520–524.
30. Sushmitha H. S, Balasubramanian Sathyamurthy. "In Silico drug designing studies on Dengue Capsid Protein". *World Journal of Pharmaceutical and Life Sciences*, 2018; 4(9): 157–161.