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IN SILICO STUDIES ON DENGUE AND SWINE FLU (INFLUENZA A) VIRAL PROTEINS WITH SELECTED *MURRAYA KOENIGII* LEAVES CONSTITUENTS

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ABSTRACT

Murraya koenigii belongs to family Rutaceae. The leaves of *Murraya koenigii* are used as herbs in Ayurvedic medicine. They are believed to possess anti-diabetic, anti microbial, anti inflammatory properties. The GCMS results showed the presence of 5 compounds in *Murraya koenigii* with a wide variety of biological activities. The comparative study of both 2 structural and 5 non-structural proteins for dengue along with 7structural and 2 non-structural proteins for Swine flu virus was carried out through In Silico methods. In this study we examined the binding affinities of 5 ligands with 14 proteins of both viruses. By our virtual screening and molecular docking result, we found that the 1,5 -Diformyl-2,6-Dimethoxy-Anthracene had the highest binding affinities with all the 14 proteins and we also predicted the binding site amino acid residues and the type of hydrogen bonding.

KEYWORDS: Molecular docking, Dengue virus, Swine flu virus, *Murraya koenigii*, Hydrogen bond.

1. INTRODUCTION

The use of plant extracts and phytochemicals, both with known antimicrobial properties, can be of very great significance in the therapeutic treatments.[1] From the time immemorial,

human civilizations are using various plants and plant products to cure the deadly diseases. The use of plants and their parts as an ethno-medicine for the treatment of various diseases is a common practice.[2] The nature of bioactive compounds in medicinal plants and their activities are influenced by genetic and environmental factors including geographical locations.[3] Curry leaves are popular leaf-spice used in very small quantities for their distinct aroma and their ability to improve digestion. Curry leaf (*Murraya koenigii*) is an important leafy vegetable. Curry leaf is also used in many of the Indian ayurvedic and unani prescriptions.[4] *Murraya koenigii* belongs to family *Rutaceae*, the fresh leaves of *Murraya koenigii* are a good source of β-carotene. Curry leaves are a rich source of Ca, K, Mg, P, along with Fe, Mn, Se and Zn, in trace amounts. The *Murraya koenigii* contains muconicine, mahanimbine, koenimbine, isomahanimbine, koenine, koenigine and koenidine which have bioactive functions like anticancer, antidiabetic, anti–oxidative and antiulcer. Curry leaves contribute a strong promising action against cardiovascular disorders, hypertension and obesity.[5]

GC-MS chromatogram of the methanolic extract of Murraya koengii (Figure-1) showed five peaks indicating the presence of five compounds. The chemical compounds identified in the methanolic extract of the leaves of *Murraya koengii* revealed the presence of α.-Caryophyllene, 2-phenyl-4–quinolinecarboxamide, Phenanthrene, 10H-Phenoxaphosphine, 1,5 -Diformyl-2,6-Dimethoxy-Anthracene.[6] α.-Caryophyllene is effective in reducing platelet activating factor-, bradykinin–and ovoalbumin-induced mouse paw oedema.[7] 2-phenyl-4–quinolinecarboxamide is a Novel Class of Potent and Selective Non-Peptide Competitive Antagonists for the Human Neurokinin-3 Receptor[8], Phenanthrene is a known irritant found in cigarette smoke, photosensitizing skin to light, 10H-Phenoxaphosphine, 1,5–Diformyl-2,6-Dimethoxy-Anthracene is reported to have anti–oxidative, antimicrobial, anti ulcer, and cholesterol reducing activities.

Dengue is a mosquito-borne systemic viral infection caused by any of the four antigenically related dengue viruses (DENV).[9] There are two well defined manifestations of dengue virus infection in humans, dengue fever and severe dengue (dengue hemorrhagic fever / dengue shock syndrome, DHF/DSS).[10] DENV is a positive-sense, single-stranded RNA virus with ~10.6kb genome.[11] There are seven non-structural proteins. Capsid protein which is responsible for gathering the viral RNA into a nucleocapsid that forms the core of a mature virus particle.[12] Envelop protein mediates virus entry into cells via interaction with a range

of cell-surface receptor molecules.[13] NS1 protein attaches to plasma membrane of cells during infection.[14] NS2A 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.[15] NS2B-NS3 protease is a crucial enzyme for the viral replication. This protein is heterodimeric protein of NS2B and NS3 protein.[16] NS3 helicase is also called as NS3 ATPase[17], a multi-domain dengue virus replication protein.[18] NS5 protein consists of Methyl Transferase [MTase] and RNA-dependent RNA polymerase [RdRp] domains, which catalyzes 5'–RNA capping/methylation and RNA synthesis, respectively, during viral genome replication.[19]

Swine flu (swine influenza) is a respiratory disease caused by viruses influenza virus that infect the respiratory tract of pigs and result in nasal secretions, a barking-like cough, decreased appetite and listless behaviour. Influenza-A (Earlier know as swine flu) is a new influenza virus causing illness in people "Influenza-A (H1N1) virus." quadruple reassortant" virus.[20] Swine influenza is known to be caused by influenza A subtypes like H1N1, H1N2, H2N3, H3N1, and H3N2. In pigs, three influenza A virus subtypes (H1N1, H1N2, and H3N2) are the most common strains worldwide.[21] Virulence and pathogenecity of influenza virus greatly varies with its surface glycoproteins such as neuraminidase (NA) and hemagglutinin (HA), NAs are nine in number while haemagglutinin proteins (HA) are sixteen in number, Other proteins of influenza A viruses include, nucleoprotein (NP), two types of matrix proteins i.e. M1 and M2, two non-structural proteins, i.e. NS1 and NS2 also called as nuclear export proteins (NEP), polymerase subunit (PA), PB1, PB1-F2 and PB2.Influenza hemagglutinin (HA) is a glycoprotein, presented on the surface of virus, The NA is glycoprotein and it is involved in antigenic variations such as antigenic drift or shift, NP is positively charged, basic protein, present in 5th segment of mRNA required for replication of virus, The M1 has L domain motif that has important role in the assembly of viral part and budding of virus, M2 is important for replication of virus at lower levels, PA is phosphoprotein and functions as protease, PB2 has role in viral transcription via N terminal and is a cap binding protein,PB1 has effect on replication, PB1-F2 is involved in forming protein channels in mitochondrial membrane, NS1 protein has many functions with respect to virulence, NS2 along with M1 participates in viral RNPs nuclear export.[22]

The utility of mathematics, computer and statistics to analyse the biological data is Bioinformatics which is an interdisciplinary branch of science. Protein Data Bank (PDB) is a

bioinformatic tool which stores the structures of proteins, ligands and macromolecules. Docking analysis can be conducted to analyse the fitness and interaction between the protein and the ligand in the form of energy. This interaction can be used as a pharmaceutical basis for drug production.[23]

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

2. MATERIALS AND METHODOLOGIES

2.1.Preparation of Dengue 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 virus were used for this study. The 3D structure of all the seven proteins were downloaded from PDB and saved in PDB format. The downloaded proteins were viewed in Py-Mol viewer.[23]

2.2. Preparation of ligands

Ligands selected were from the previous studies on GCMS analysis on Murraya koengii leaves extract.[6] 5 ligands were used for the study. Ligands were constructed using Chem Sketch.[23] 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.[17] 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 Swine flu viruses proteins with 5 ligands.

Table 1: The Total Binding Energy (kcal/mol) profile for Dengue and swine flu virus non structural proteins with 5 ligands.

Ligand	Compound name	Dengue Virus					Swine flu Virus	
		NS1 protein	Trans membrane domain of NS2A	NS2B / NS3 protease	NS3 helicase	NS5 protein	NS1	NS2 [NEP M1–Binding Domain]
A	Alpha-Caryophyllene	-68.5	-59.4	-58.2	-71.4	-66.1	-62	-58.1
B	2-Phenyl-4-Quinolinecarboxamide	-98.1	-81.4	-103.7	-94.5	-97.7	-87.6	-84.9
C	Phenanthrene	-85.3	-60.7	-68.2	-80.8	-79.6	-72.8	-59.1
D	10H-Phenoxaphosphine	-83.3	-61.6	-70.3	-73.8	-74.5	-67.3	-58.8
E	1,5-Diformyl-2-6-Dimethoxy-Anthracene	-99.3	-87.3	-106.4	-99.9	-112.8	-92.7	-75.2

Table 2: The Total Binding Energy (kcal/mol) profile for Dengue and Swine flu virus structural proteins with 5 ligands.

Ligand	Compound name	Dengue Virus		Swine flu Virus						
		Capsid protein	Envelope protien	Nucleoprotein	M1–Matrix protein	HA	NA	PA	PB 2	PA-PB1 complex
A	Alpha-Caryophyllene	-59.7	-57.7	-73.5	-61.4	-57.1	-54.9	-60	-57.8	-64.8
B	2-Phenyl-4-Quinolinecarboxamide	-89.4	-89.8	-94.8	-97.2	-89.8	-92.3	-91	-82.3	-93.8
C	Phenanthrene	-78.1	-60	-85.1	-73.2	-66.5	-71.1	-63	-68.2	-66.7
D	10 H-Phenoxaphosphine	-76.1	-61.3	-79.9	-73.8	-69.1	-69	-68.2	-56.4	-64.5
E	1,5-Diformyl-2-6-Dimethoxy-Anthracene	-85.9	-94.9	-100.1	-102.8	-92.5	-97.1	-89.8	-82.1	-95.3

3.2 H–Bond profile for Dengue and Swine flu viruses protein with 5 ligands:

Table 3: H–Bond profile for Dengue and swine flu virus non structural proteins with 5 ligands.

Ligand	Compound name	Dengue Virus					Swine flu Virus	
		NS1 protein	Trans membrane domain of NS2A	NS2B / NS3 protease	NS3 helicase	NS5 protein	NS1	NS2 [NEP M1–Binding Domain]
A	Alpha-Caryophyllene		-	-	-	-	-	-
B	2-Phenyl-4-Quinolinecarboxamide	H-M H-M	H-M	H-S H-M	H-M H-S	H-M H-S	H-S -	- -
C	Phenanthrene	-	-	-	-	-	-	-
D	10 H-Phenoxaphosphine	-	-	-	-	-	-	-
E	1,5-Diformyl-2-6-Dimethoxy-Anthracene	H-M H-S	H-M H-S	H-M H-S	H-M H-S	H-M H-S	H-M H-M	H-S

Table 4: H–bond profile for Dengue and swine flu virus structural proteins with 5 ligands.

Ligand	Compound name	Dengue Virus		Swine flu Virus						
		Capsid protein	Envelope protien	Nucleoprotein	M1–Matrix protein	HA	NA	PA	PB 2	PA-PB1 complex
A	Alpha-Caryophyllene	-	-	-	-	-	-	-	-	-
B	2-Phenyl-4-Quinolinecarboxamide	H-M	H-M	H-M H-S	H-M	H-M H-S	H-M	H-M	H-M H-S	H-M H-S
C	Phenanthrene	-	-	-	-	-	-	-	-	-
D	10 H-Phenoxaphosphine	-	H-S	H–S	-	-	-	H-S	-	H-S
E	1,5-Diformyl-2-6-Dimethoxy-Anthracene	H-S	H-M H-S	H-S		H-S	H-M H-S	H-S	H-M H-S	H-M H-S

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

Table 5: Amino acid position profile for Dengue and Swine flu virus non structural proteins with 5 ligands.

Ligand	Compound name	Dengue Virus					Swine flu Virus	
		NS1 protein	Trans membrane domain of NS2A	NS2B / NS3 protease	NS3 helicase	NS5 protein	NS1	NS2 [NEP M1–Binding Domain]
A	Alpha-Caryophyllene	-	-	-	-	-	-	-
B	2-Phenyl-4-Quinolinecarboxamide	Ile(224)	Gly(3)	Leu(149) Asn(152) Ala(164)	Leu(193)	Met(342) Asp(344)	Arg(44)	-
C	Phenanthrene	-	-	-	-	-	-	-
D	10H-Phenoxaphosphine	-	-	-	-	-	-	-
E	1,5-Diformyl-2-6-Dimethoxy-Anthracene	Ile(243)	Gly(3) Leu(11)	Gly(87)	Ser(321)	Asn(69)	His(17) Arg(44)	Gln(71)

Table 6: Amino acid profile for Dengue and Swine flu virus structural proteins with 5 ligands.

Ligand	Compound name	Dengue Virus		Swine flu Virus						
		Capsid protein	Envelope protien	Nucleoprotein	M1–Matrix protein	HA	NA	PA	PB 2	PA-PB1 complex
A	Alpha-Caryophyllene	-	Ile (616) Val(626) Gly(628) Arg(629) Ile (630)	-	-	-	-	-	-	-
B	2-Phenyl-4-Quinolinecarboxamide	Leu(29) Leu(46)	-	Arg(152)	Asn(36) Asp(38)	Arg (124)	Arg(368) Ser(400)	Glu(424) Lys(488)	Thr(612)	Pro(325) Glu(327) Glu(538)
C	Phenanthrene	-	Arg(672)	-	-	-	-	-	-	-
D	10 H-Phenoxaphosphine	-	Ile (630)	Asp(160)	-	-	-	Asn(466)	-	Trp (577)
E	1,5-Diformyl-2-6-Dimethoxy-Anthracene	Arg (68)		Glu(81)	Ser (53)	Asn (129)	Thr (81) Val(410)	Asn(466)	Arg(604)	Arg (279)

4 DISCUSSION

Considering all the tables from Table–1 to Table–6, the 3D structure coordinates of seven proteins of dengue and nine proteins of Swine flu viruses are optimized and 5 compounds from Murraya koengii leaves extract are identified. The total binding energy of the compounds with all the sixteen proteins was calculated using iGEMDOCK. Evaluations of binding conformation of these 5 compounds with seven dengue and 9 Swine flu viral proteins are performed using iGEMDOCK. From docking study, we listed binding affinities of 5 compounds based on ligand binding energy (Table.1 and 2). The binding pose for each ligand molecule into the dengue and Swine flu 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 "E" is found to have lower ligand binding energy (binding energy value= -94.9 kcal/mol), than other analogs for Envelope protein. Compound "B" has least binding energy score with caspid protein (binding energy value= -89.4 kcal/mol), the structural proteins of Swine flu virus had following binding energies, Nucleoprotein('E' binding energy value= -100.1kcal/mol), M1 Matrix protein('E' binding energy value= -102.8), HA('E', binding energy value= -92.8kcal/mol), NA Glycoprotein('E', binding energy value= -97.1kcal/mol),PA protein('B' binding energy value= -91kcal/mol),PB2('B' binding energy value= -82.3kcal/mol), PA-PB1 complex('E' binding energy value= -95.3kcal/mol). The non structural proteins of Dengue virus had these binding energy values: Trans membrane domain of NS2A ('E', binding energy value= -87.3kcal/mol), NS2B / NS3 protease ('E', binding energy value= -106.4kcal/mol), NS3 helicase ('E', binding energy value= -99.9kcal/mol), NS5 protein ('E', binding energy value= -112.8 kcal/mol) and NS1 protein ('E', binding energy value = -99.3kcal/mol). And the non structural proteins of Swine flu viruses have, NS1 ('E', binding energy value= -92.7kcal/mol), NS2 ('B', binding energy value= -84.9kcal/mol). We found that the compound "E" was found to have the best binding affinity with seven dengue and nine Swine flu viral proteins.

4.1 Non-Structural proteins of Dengue Virus

4.1.1. The Total Binding Energy for Dengue virus NS1 protein with 5 ligands:

From Table–1, Table–3 and Table–5, the docking simulation of 5 ligands were performed for Dengue virus NS1 protein. From the docking study, we observed that compound–E has best binding affinity with the target NS1 protein with the binding energy value of -99.3 kcal/mol.

Interaction analysis of binding mode of compound–E in dengue virus NS1 protein reveals that it forms two hydrogen bond with low energy with Ile (243) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus NS1 protein with 5 ligands: is shown in Fig.1.

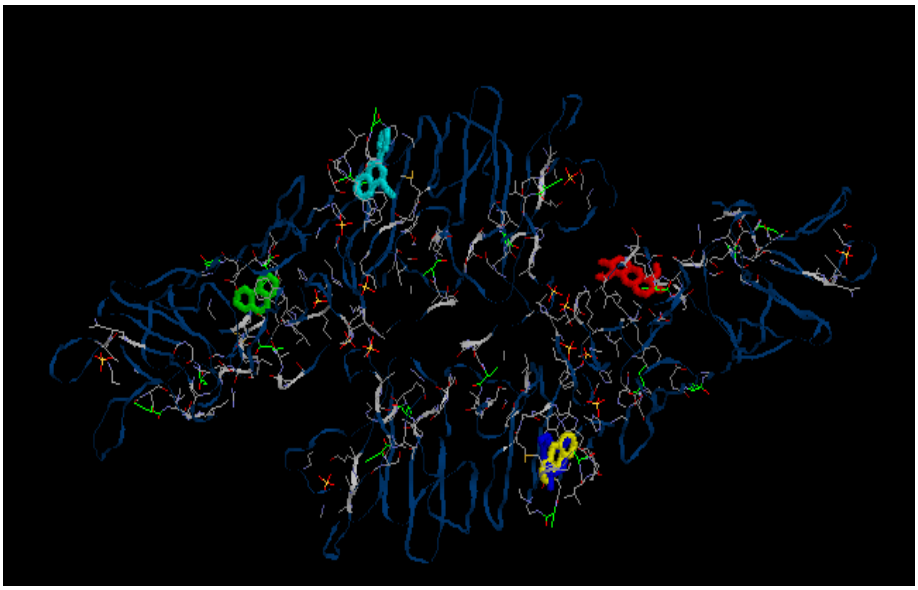

Fig.1: The Total Binding profile for Dengue virus NS1 protein with 5 ligands.

4.1.2. The Total Binding Energy for Dengue virus Transmembrane domain of NS2A with 5 ligands.

From Table–1, Table–3 and Table–5, the docking simulation of 5 ligands were performed for Dengue virus Transmembrane domain of NS2A. From the docking study, we observed that compound–E has best binding affinity with the target Trans membrane domain of NS2A with the binding energy value of -87.3 kcal/mol. Interaction analysis of binding mode of compound–E in dengue virus NS2A protein reveals that it forms two hydrogen bond with low energy one with Gly(3) and other with leu(11) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus Trans membrane domain of NS2A with 5 ligands: is shown in Fig.2.

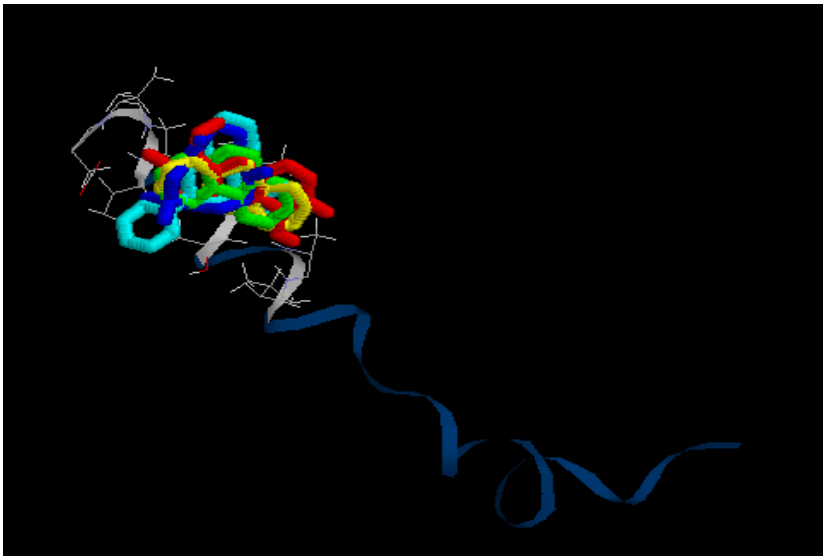

Fig.2: The Total Binding profile for Dengue virus Trans membrane domain of NS2A with 5 ligands.

4.1.3. The Total Binding Energy for Dengue virus NS2B / NS3 protease with 5 ligands:

From Table–1, Table–3 and Table–5, the docking simulation of 5 ligands were performed for Dengue virus NS2B / NS3 protease. From the docking study, we observed that compound–E has best binding affinity with the target NS2B / NS3 protease with the binding energy value of -106.4 kcal/mol. Interaction analysis of binding mode of compound–E in dengue virus NS2B / NS3 protease reveals that it forms two hydrogen bond with low energy, with Gly(87) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus NS2B / NS3 protease with 5 ligands: is shown in Fig.3.

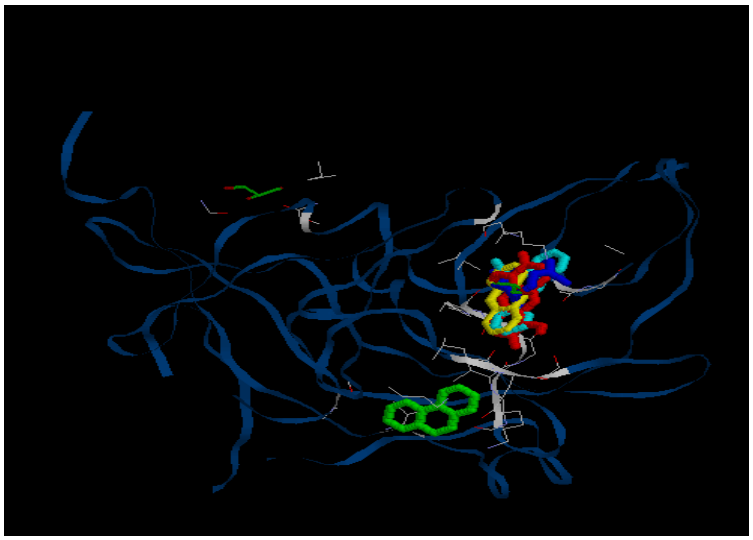

Fig.3: The Total Binding profile for Dengue virus NS2B / NS3 protease with 5 ligands.

4.1.4. The Total Binding Energy for Dengue virus NS3 helicase with 5 ligands

From Table–1, Table–3 and Table–5, the docking simulation of 5 ligands were performed for Dengue virus NS3 helicase. From the docking study, we observed that compound–E has best binding affinity with the target NS3 helicase with the binding energy value of -99.9 kcal/mol. Interaction analysis of binding mode of compound–E in dengue virus NS3 helicase reveals that it forms two hydrogen bonds with low energy, with Ser(321) residues. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus NS3 helicase with 5 ligands: is shown in Fig.4.

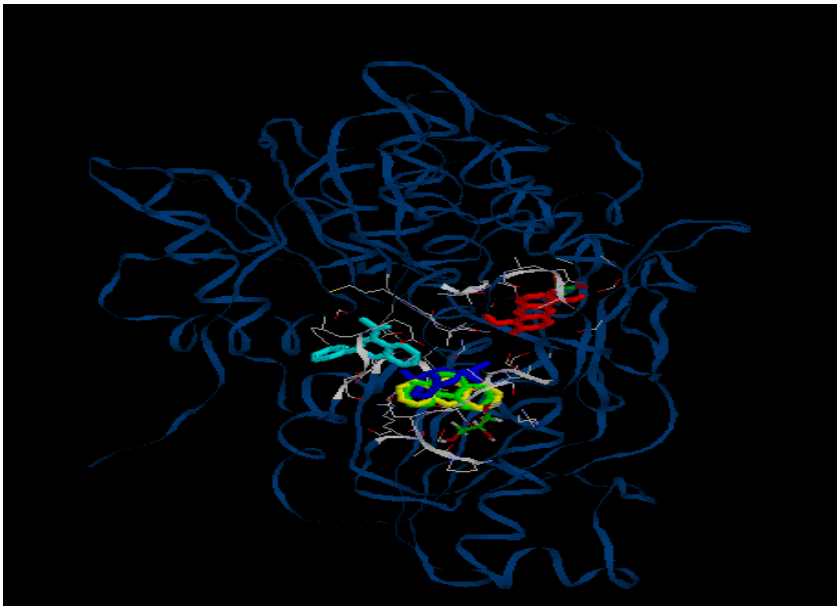

Fig.4: The Total Binding profile for Dengue virus NS3 helicase with 5 ligands.

4.1.5. The Total Binding Energy for Dengue virus NS5 protein with 5 ligands

From Table–1, Table–3 and Table–5, the docking simulation of 5 ligands were performed for Dengue virus NS5 protein. From the docking study, we observed that compound–E has best binding affinity with the target NS5 protein with the binding energy value of -112.8kcal/mol. Interaction analysis of binding mode of compound–E in dengue virus NS5 protein reveals that it forms two hydrogen bonds with low energy, with Asn (69) residues. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus NS5 protein with 5 ligands: is shown in Fig.5.

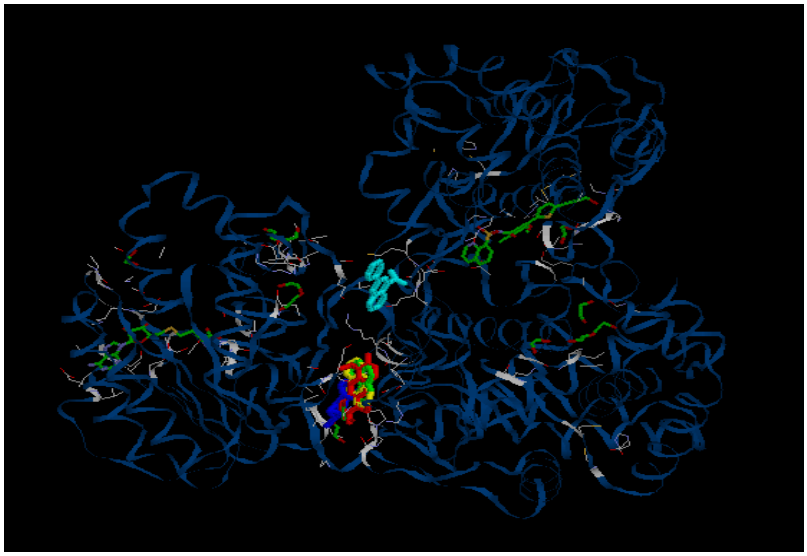

Fig.5: The Total Binding profile for Dengue virus NS5 protein with 5 ligands.

4.2 Non-Structural proteins of Swine flu Virus

4.2.1. The Total Binding Energy for Swine flu NS1 protein with 5 ligands

From Table–1, Table–3 and Table–5, the docking simulation of 5 ligands were performed for Swine virus NS1 protein. From the docking study, we observed that compounds–E has best binding affinity with the target NS1 protein with the binding energy values of -92.7 kcal/mol. Interaction analysis of binding mode of compounds–E in dengue virus NS1 protein reveals that it forms two hydrogen bond with low energy, with His(17), Arg(44) and residues. A close-up view of the Total Binding Energy (kcal/mol) profile for Swine flu virus NS1 protein with 5 ligands: is shown in Fig.6.

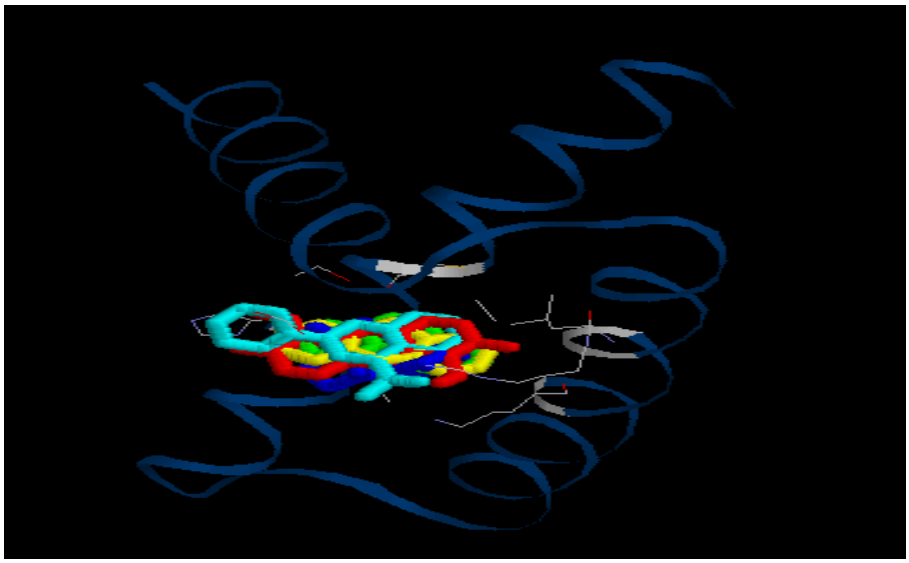

Fig.6: The Total Binding profile for Swine flu virus NS1 protein with 5 ligands.

4.2.2. The Total Binding Energy for Swine flu virus NS2 protein with 5 ligands

From Table–1, Table–3 and Table–5, the docking simulation of 5 ligands were performed for Swine flu virus NS2 protein. From the docking study, we observed that compound–B has best binding affinity with the target NS2 protein with the binding energy value of -84.9kcal/mol. A close-up view of the Total Binding Energy (kcal/mol) profile for Swine flu virus NS2 protein with 5 ligands: is shown in Fig.7.

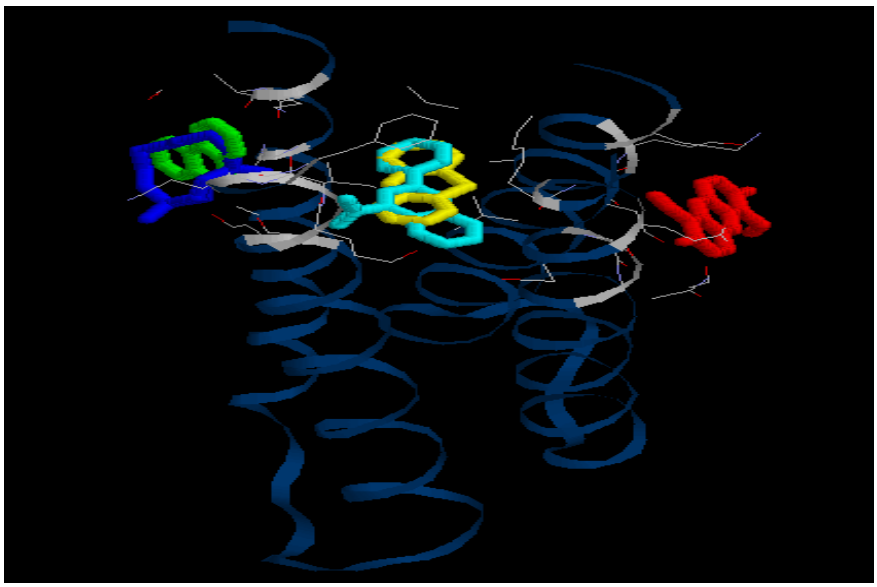

Fig.7: The Total Binding profile for Swine flu viral protein with 5 ligands.

4.3 Structural proteins of Dengue virus

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

From Table–2, Table–4 and Table–6, the docking simulation of 5 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 -89.4 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 Leu(29) and Leu(46) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus Capsid protein with 5 ligands: is shown in Fig.8.

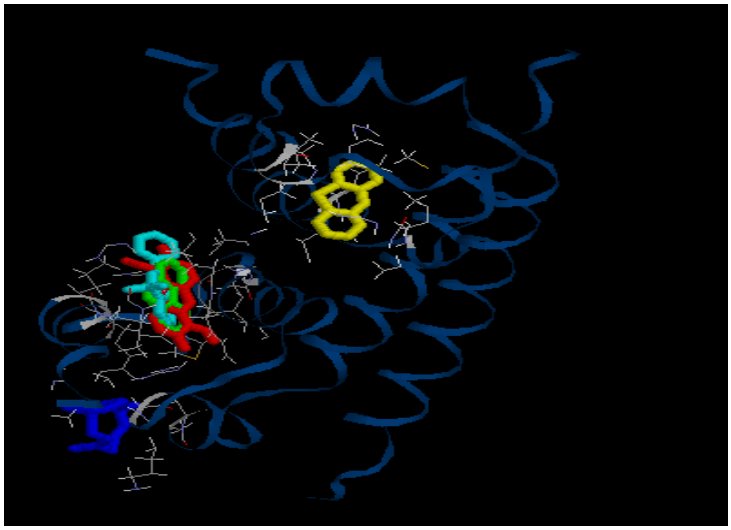

Fig.8: The Total Binding profile for Dengue virus Capsid protein with 5 ligands.

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

From Table–2, Table–4 and Table–6, the docking simulation of 5 ligands were performed for Dengue virus envelope protein. From the docking study, we observed that compound–E has best binding affinity with the target envelope protein with the binding energy value of -94.9 kcal/mol. Interaction analysis of binding mode of compound–E in dengue virus envelope protein reveals that it forms two hydrogen bond with low energy, with Ile(630) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus envelope protein with 5 ligands: is shown in Fig.9.

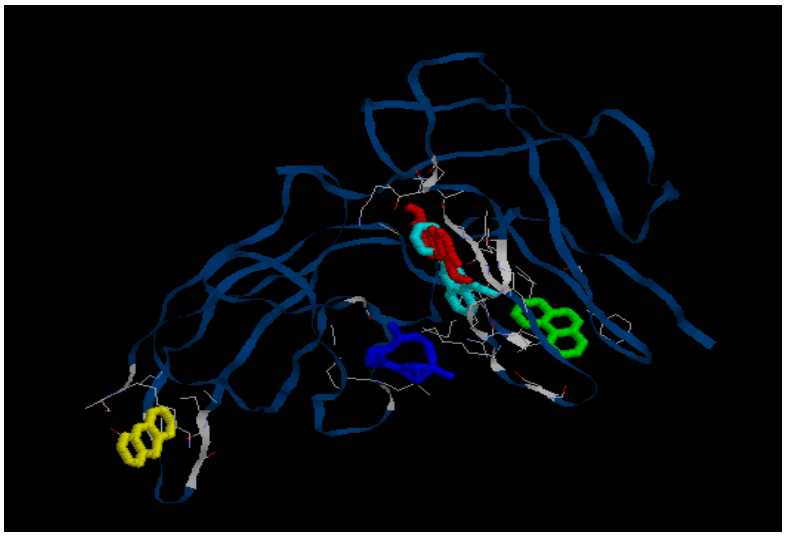

Fig.9: The Total Binding Energy (kcal/mol) profile for Dengue virus envelope protein with 5 ligands.

4.4.Structural proteins of Swine flu virus

4.4.1. The Total Binding Energy for Swine flu virus Nucleoprotein protein[NP] with 5 ligands.

From Table–2, Table–4 and Table–6, the docking simulation of 5 ligands were performed for Swine flu virus Nucleoprotein. From the docking study, we observed that compound–E has best binding affinity with the target Nucleoprotein with the binding energy value of -100.1 kcal/mol. Interaction analysis of binding mode of compound–E in dengue virus Nucleoprotein reveals that it forms one hydrogen bond with low energy, with Glu(81) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Swine flu virus Nucleoprotein with 5 ligands: is shown in Fig.10.

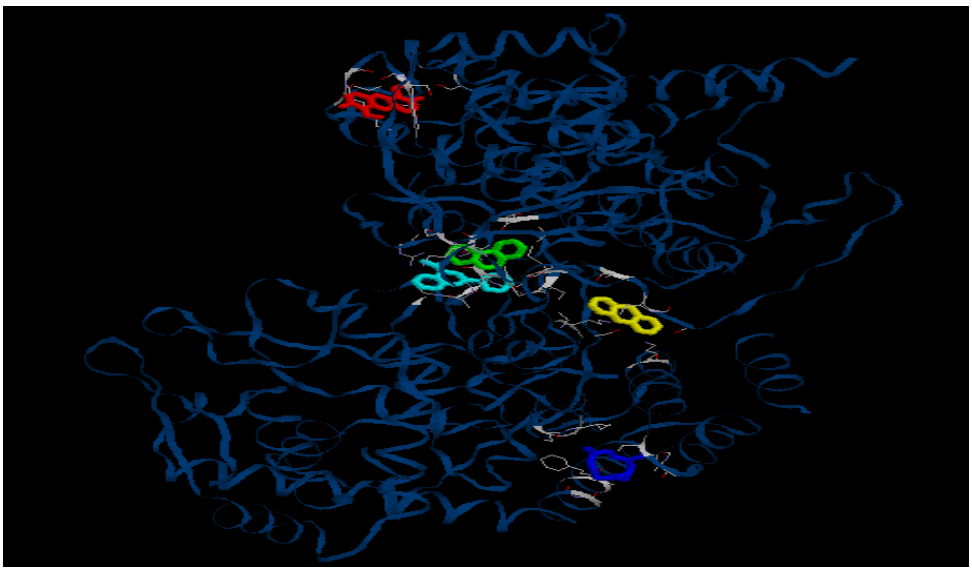

Fig.10: The Total Binding profile for Swine flu virus nucleoprotein with 5 ligands.

4.4.2. The Total Binding Energy for Swine flu virus M1–Matrix protein with 5 ligands.

From Table–2, Table–4 and Table–6, the docking simulation of 5 ligands were performed for Swine flu virus M1 Matrix protein. From the docking study, we observed that compound–E has best binding affinity with the target M1 Matrix protein with the binding energy value of -102.8 kcal/mol. Interaction analysis of binding mode of compound–E in dengue virus M1 Matrix protein reveals that it forms two hydrogen bonds with low energy, with Ser(53) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Swine flu virus M1 Matrix protein with 5 ligands: is shown in Fig.11.

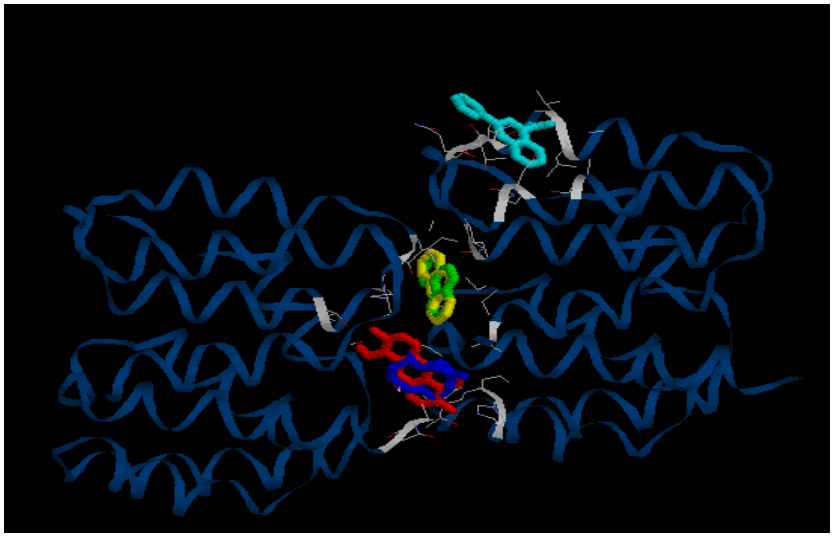

Fig.11: The Total Binding profile for Swine flu virus M1 Matrix protein with 5 ligands

4.4.3. The Total Binding Energy for Swine flu virus glycoprotein[HA] protein with 5 ligands.

From Table–2, Table–4 and Table–6, the docking simulation of 5 ligands were performed for Swine flu virus HA Nucleocaspid protein. From the docking study, we observed that compound–E has best binding affinity with the target glycoprotein [HA] protein with the binding energy value of -92.8 kcal/mol. Interaction analysis of binding mode of compound–E in dengue virus glycoprotien [HA] protein reveals that it forms one hydrogen bond with low energy, with Asn(129) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Swine flu virus glycoprotein [HA] protein with 5 ligands: is shown in Fig.12.

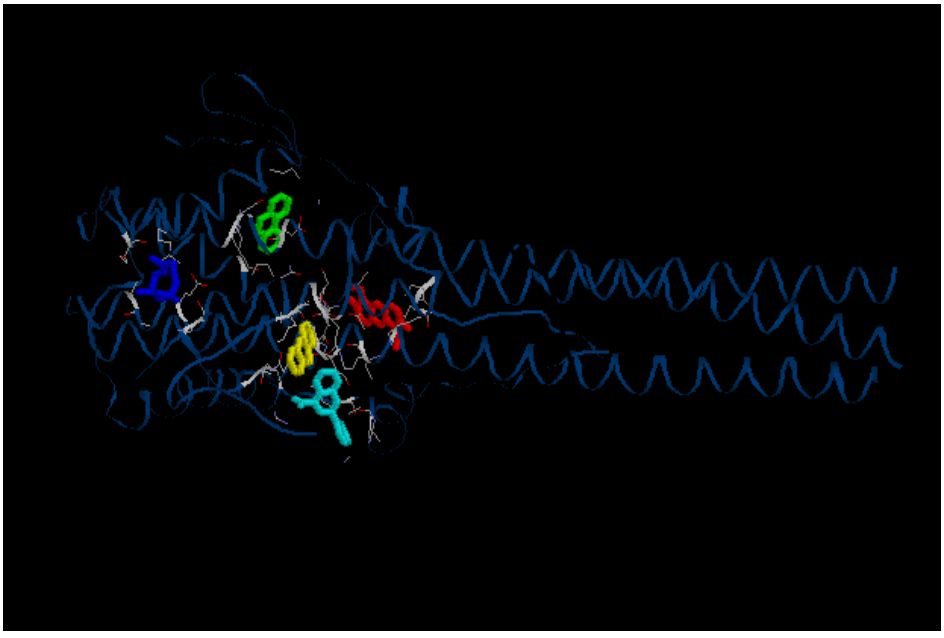

Fig.12: The Total Binding for Swine flu virus glycoprotein [HA] protein with 5 ligands

4.4.4. The Total Binding Energy for Swine flu virus Neuraminidase protien with 5 ligands.

From Table–2, Table–4 and Table–6, the docking simulation of 5 ligands were performed for Swine flu virus Neuraminidase [NA] glycoprotien protein. From the docking study, we observed that compound–E has best binding affinity with the target with the binding energy value of -97.1kcal/mol. Interaction analysis of binding mode of compound–E in dengue virus Neuraminidase [NA] glycoprotein reveals that it forms two hydrogen bond with low energy, with Thr (81) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Swine flu virus Neuraminidase [NA] glycoprotein with 5 ligands: is shown in Fig.13.

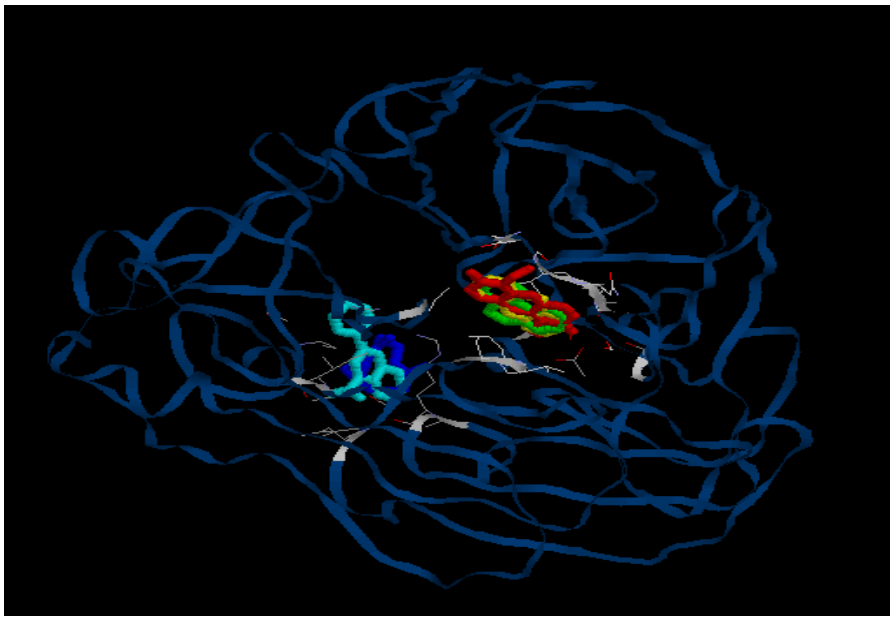

Fig.13: The Total Binding profile for Swine flu virus Neuraminidase glycoprotein protein with 5 ligands.

4.4.5. The Total Binding Energy for Swine flu virus polymerase protien with 5 ligands

From Table–2, Table–4 and Table–6, the docking simulation of 5 ligands were performed for Swine flu virus PA protein. From the docking study, we observed that compound–B has best binding affinity with the target polymerase with the binding energy value of -91kcal/mol. Interaction analysis of binding mode of compound–B in dengue virus polymerase reveals that it forms one hydrogen bond with low energy, with Glu (424) and Lys (488) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Swine flu polymerase with 5 ligands: is shown in Fig.14.

Fig.14: The Total Binding profile for Swine flu virus PA protein with 5 ligands.

4.4.6. The Total Binding Energy for Swine flu virus polymerase [PB2]protien with 5 ligands

From Table–2, Table–4 and Table–6, the docking simulation of 5 ligands were performed for Swine flu virus PB2 protein. From the docking study, we observed that compound–B has best binding affinity with the target polymerase with the binding energy value of -91.7kcal/mol. Interaction analysis of binding mode of compound–B in dengue virus polymerase reveals that it forms two hydrogen bond with low energy, with Thr (612) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Swine flu PB2 with 5 ligands: is shown in Fig.15.

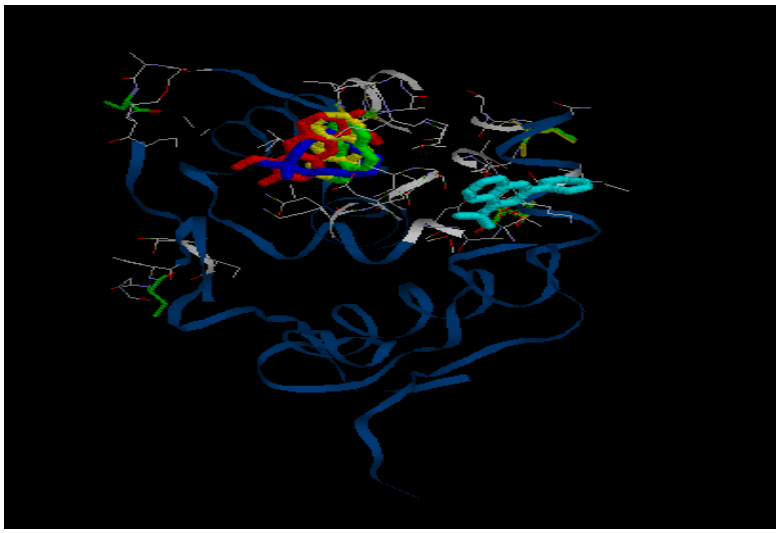

Fig.15: The Total Binding profile for Swine flu virus PB2 protein with 5 ligands.

4.4.7. The Total Binding Energy for Swine flu virus PA-PB2 with 5 ligands

From Table–2, Table–4 and Table–6, the docking simulation of 5 ligands were performed for Swine flu virus PA-PB1 protein. From the docking study, we observed that compound–E has best binding affinity with the target polymerase with the binding energy value of -95.3kcal/mol. Interaction analysis of binding mode of compound–E in dengue virus polymerade reveals that it forms two hydrogen bond with low energy, with Arg (279) residue. A close-up view of the Total Binding Energy (kcal/mol) profile for Swine flu virus polymerase with 5 ligands: is shown in Fig.16.

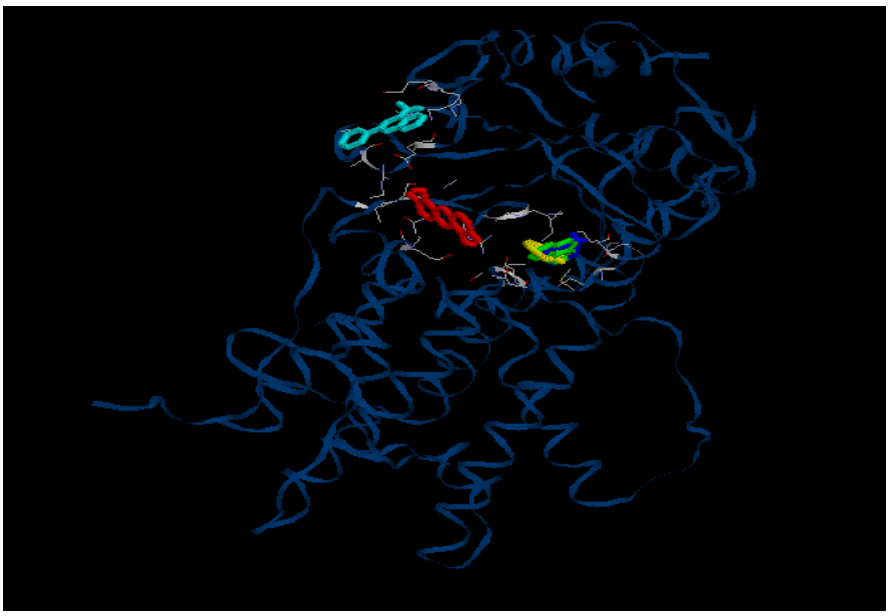

Fig.16: The Total Binding profile for Swine flu virus PA-PB1 Complex protein with 5 ligands.

5. CONCLUSION

Our molecular docking studies explored the possible binding modes of 5 compounds that are present in *Murraya koengii* leaf with seven proteins of Dengue virus and 9 proteins of Swine flu virus. Dengue virus consists of envelope protein, NS1 protein, Transmembrane domain of NS2A, NS2B/NS3 protease, NS3 helicase, NS5 protein and capsid protein; Swine flu virus consists of NS1, NS2/NEP, NP Nucleoprotein, M1 Matrix protein, HA and NA glycoprotein, PA, PB2, and PA-PB1 complex. It revealed that all the 5 compounds show minimum affinity with all the proteins. The compound ‘E’ (1, 5-Diformyl-2-6-Dimethoxy-Anthracene) showed the 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 'E' has highest binding affinity with most of the structural proteins of Dengue virus and Swine flu virus. Whereas the compound 'B' (2-Phenyl-4-Quinolinecarboxamide) and 'E' (1, 5-Diformyl-2-6-Dimethoxy-Anthracene) is shown to have highest binding affinity with most of the non structural proteins of Dengue virus and the non structural proteins of Swine flu virus has highest binding affinities with both 'B' and 'E' compounds and therefore it can be used as an effective drug target for Dengue virus as well as Swine flu virus. Hence, the Compound 'E' may be considered as the effective drug target for both dengue and swine flu 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 probably the first such 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 Swine flu.

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