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DOCKING STUDY OF SELECTED *RED VITIS VINIFERA* PULP CONSTITUENTS ON DENGUE VIRAL PROTEINS – AN *IN SILICO* APPROACH

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ABSTRACT
Grape Red *Vitis Vinifera* (Manto Negro Red Grape) belonging to family *vitaceae* is one of the most economically important plant, widely cultivated and consumed fruits as they rich in the phtyochemicals like phenolic acids, stilbenes, anthocyanins, and proanthocyanidins which are strong antioxidants. The compositions of phytochemicals in grapes however, vary greatly among the different varieties. The sugars and the organic acids present in the grape are important phytochemicals responsible to the nutrition and sensory properties of the fruits. In this study, we have carried out the binding efficiency of 18 compounds present in the Red *Vitis Vinifera* with the seven non structural dengue virus proteins through in silico methods. By virtual screening and docking result, we have found that 2, 6-piperazinedione, dioxime and Succinic acid, hex-4-yn-3-yl propyl ester has highest binding affinity for these proteins.

KEYWORDS: *Vitis Vinifera*, Phytochemicals, Binding interaction, molecular docking, hydrogen bond.

1. INTRODUCTION
The word "Herb" was derived from Latin word "herba" and an old French word " herbe", These days it refers to part of the plants like seed, stem, bark, flower, leaf, stigma or a root and non-woody plant unlike olden days where herb was applied to only non-woody plants. Ancient Unani manuscripts, Egyptian papyrus, and Chinese writings described the use of herbs as medicine. India has been known to be rich repository of medicinal plants since ancient civilizations. Treatment with herbs is considered to be safe mainly the reason being no or minimal side effects. Native healers often claim to have learned by observing that sick animals change their food preferences to nibble at bitter herbs they would normally reject. Herbs are considered as rich resources of ingredients which are used in pharmacopoeial and non-pharmacopoeial or synthetic drugs. Plant synthesizes a variety of phytochemicals.[1]

Red *Vitis Vinifera*, a species of *vitis*, consists of the sub-genera *Euvitis* and *Muscadinia* and together with 11–13 other genera belongs to the family *Vitaceae* which is eaten fresh, processed to make wine, juice and dried to produce raisins. Due to its regenerative ability it was considered as a symbol of life, thus frequently referred to as the tree of life. The Polyphenols, also known as phenolics, contain phenol rings, anthocyanins that give grapes their purple color. The phytochemical composition and the health beneficial effects of various phenolic compounds found in grape (*Vitis vinifera L.*) stems, has as a value-added byproduct of the winery industry. These are considered to have biological properties, not only limited to anti-oxidant, antiinflammatory, anti-cancer, antimicrobial, antiviral, cardioprotective, neuroprotective, hepatoprotective activities but also as a nutraceuticals.[2]

The GCMS chromatogram of methanolic extract of red grape pulp showed 62 compounds. Of these 62 reported, 18 compounds were choosen to find the best docking fit with different types of dengue virus proteins.[3] Those 18 compounds include 1,3,5-Triazine-2,4,6-triamine, 2-Fluoro-5-methylaniline, 2,4,5-triaminopyrimidine, 2-chloro-1,3-benzenediol, 2-naphthalenol, 4-Fluorobenzylalcohol, 2,4-dihydroxy-2,5-dimethyl-3(2H)-Furan-3-one, 2,6-Piperazinedione,dioxime, 3-Fluorobenzylalcohol, 4,5-diamino-2-hydroxypyrimidine, 4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl, 10-chlorodecyl(E)-2-methylbut-2-enoate, Butanoic acid,3-butenyl ester, Propylamine,N,N,2,2-tetramethyl-n-oxide, Propanol,2,3-dihydroxy-(S)-, Succinic acid, hex-4-yn-3-yl propyl ester, Thiophene,3-(1,1-dimethylethyl)-, Thymine 1,3,5-Triazine-2,4,6-triamine, 2,4-dihydroxy-2,5-dimethyl-3(2H)-Furan-3-one and Thymine were found to have antibacterial and antifungal properties.[3] 2-Fluoro-5-methylaniline was found to

have immunosuppressive properties. 2,4,5-triaminopyrimidine had potent activity against malaria. 2-Cholro1,3-benzenediol and Propanol 2,3-dihydroxy-(S) were found to be useful in the treatment of Cancer. 2-naphthalenol was to be useful in the treatment of skin diseases.4-Fluorobenzylalcohol, 3-Fluorobenzylalcohol and Thiophene,3-(1,1-dimethylethyl)- are potent anti-microbial and anti-inflammatory activity.2,6-piperazinedione,dioxime and Butanoic acid 3-butenyl ester had a good activity as a herbicide.4,5-diamino-2-hydroxypyrimidine is an anti-viral and anti-tumor agent. 10-chlorodecyl(E)-2-methylbut-2-enoate is used in treatment of Psoriasis. Succinic acid,hex-4-yn-3-yl propyl ester is used in treatment of Arthritis.4H-Pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl has anti-proliferative and pro-apoptotic effects.[4] However, Propylamine,N,N,2,2-tetramethyl –n-oxide has no medicinal activity reported yet.

Dengue is caused by Dengue virus (DENV), a mosquito-borne flavivirus. DENV is an single stranded RNA positive-strand virus of the family Flaviviridae, genus Flavivirus. This genus includes also the West Nile virus, Tick-borne Encephalitis Virus, Yellow Fever Virus, and several other viruses which may cause encephalitis. DENV causes a wide range of diseases in humans, from a self limited Dengue Fever (DF) to a life-threatening syndrome called Dengue Hemorrhagic Fever (DHF) or Dengue Shock Syndrome (DSS)[5]

There are four antigenically different serotypes of the virus (although there is report of 2013 that a fifth serotype has been found): Dengue is an emerging arboviral, arthropodborne disease. Dengue virus infection with 1 of 4 serotyes produces ranging clinical illness from an asymptomatic mild illness to severe forms of illness Dengue hemorrhagic fever (DHF) which is transmitted within humans through Aedes Female mosquitoes subgenus *Steqomyia*.*Ae. aeqypti* which is the most epidemic vector. Dengue vaccine development has become a challenging task due to the four serotypes each capable of eliciting cross-reactive and disease enhancing antibody response against the three remaining serotypes. Incidence of dengue fever has been increased 30 fold in last five years. The viral genome consists of positive sense of RNA which encodes for three structural proteins Capsid (c), premembrane (prM), envelop (E), and non-structural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B and NS5).[6]

Capsid protein of dengue virus is a highly basic protein of 12kDa that forms homodimers in solution with affinity for both nucleic acids and lipid membranes. Structural studies show monomer has four alpha helices. The mature capsid protein remains associated with ER membranes via hydrophobic region, which is conserved in a wide range of mosquitoes.[7] Envelope protein is a class two fusion protein, essential for receptor binding, membrane fusion, and inducing protective antibodies. This protein folds into three distinct domains (D1, D2 and D 3) that co-relate to the antigenic domains. Once the cells are infected with dengue virus, it encodes a non- structural protein 1 (NS1), a relatively conserved 45-50kDa glycoprotein. Then NS1 is secreted from the mammalian cells as soluble hexamer.NS1 in their folded state serve to deliver optimal antigencity.[8] Trans membrane domain of NS2A protein is essential for viral replication and is poorly characterized by membrane protein. It displays both protein-protein and protein-membrane interactions this may be involved in membrane rearrangements.[9] NS2B\NS3 protease is translated as a single polyprotein precursor, which must be cleaved into individual proteins by host protease. This step of cleavage is obligate step of viral life cycle. NS3 helicase protein is Mg^{2+} dependent and responsible for replication by unwinding the duplex RNA utilizing the chemical energy derived by ATP hydrolysis.[10] Non structural protein 5 (NS5) consists of methyl transferase and RNA dependent RNA polymerase domains, which catalyze methylation and replication. These interactions are maintained by intermolecular interactions.[11]

Bioinformatics is an interdisciplinary field mainly involves genetics, molecular biology, mathematics, statistics which addresses the biological problems in the computational point of view.[12] The Protein Data Bank (PDB) which is the single global repository for experimentally determined 3D structures of biological macromolecules and their complexes with ligands which consists of >130000 structures determined by macromolecular crystallography, NMR and electron cryo-microscopy.[13,14] Recently developed wwPDB tool for deposition, validation of biological macromolecules which allows efficient and effective usage by research scientists, students and the curious public world wide. Docking analysis can be conducted for the protein and the ligand to analyse the fitness and the interaction with each other in the form of energy. This interaction could be used as the pharmaceutical approach for drug production.[15]

The aim of our study is to find the best docking fit from the selected 18 compounds of Red *vitis vinifera* extract with seven different non structural Dengue 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. Seven 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.[16]

2.2. Preparation of ligands

Ligands selected were from the previous studies on GCMS analysis on *Calotropis gigantea* leaves extract. 5 ligands were selected based on the retention area exhibited on GCMS and those were used for this docking study. Selected 5 ligands were constructed using Chem Sketch.[17] 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.[22] 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 each individual 5 ligands were 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[18]

3. RESULTS

3.1. Total Binding Energy (kcal/mol) profile for Dengue viruses protein with 18 ligands.

Table 1: The Total Binding Energy (kcal/mol) profile for Dengue viral protein with 18 ligands.

Ligand	Compound name	Envelope protein	NS1 protein	Trans membrane domain of NS2A	NS2B / NS3 protease	NS3 helicase	NS5 protein	Capsidprotein
A	2,4-dihydroxy-2,5 dimethyl 3 (2H),furan-3-one	-62.3	-82.7	-394.1	-61.7	-72.0	-71.2	-73.6
B	4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy 6 methyl	-63.4	-80.9	-400.5	-63.9	-70.5	-71.5	-65.4
C	N,N,2,2-Tetramethylpropan-1-amine oxide	-47.9	-58.2	-325.6	-50.2	-54.9	-53.2	-55.4
D	1,3,5 triazine 2,4,6 triamine	-65.3	-82.6	-419.2	-71.0	-77.3	-79.7	-61.3
E	2 chloro 1,3 benzenediol	-64.6	-73.9	-378.7	-54.4	-67.0	-61.8	-57.5
F	2 flouro 5 methylaniline	-53.0	-69.5	-406.0	-52.6	-58.1	-57.8	-58.8
G	2 napthalenol	-64.5	-79.0	-415.9	-66.7	-71.1	-69.5	-69.7
H	2,4,5, triaminopyrimidine	-63.5	-76.7	-439.3	-68.9	-76.0	-78.1	-61.0
I	2,6-piperazinedione, dioxime	-75.3	-83.8	-475.9	-78.7	-88.5	-86.5	-81.3
J	3 Flouro benzyl alcohol	-59.9	-69.6	-403.4	-58.4	-61.5	-59.4	-61.5
K	4 flourobenzylalcohol	-53.9	-69.9	-401.8	-56.0	-60.4	-58.6	-62.6
L	4,5-Diamino-2-hydroxypyrimidine	-64.1	-79.1	-427.8	-63.7	-73.5	-81.1	-61.2
M	10-Chlorodecyl (E) -2-methylbut-2-enoate	-73.4	-84.0	-496.4	-76.2	-83.8	-78.1	-73.6
N	Butanoic acid 3-butenyl ester	-60.0	-67.2	-432.9	-57.5	-62.0	-61.7	-69.2
O	Propanal, 2,3-dihydroxy-, (S)-	-61.4	-65.4	-335.2	-55.3	-62.6	-59.4	-55.0
P	Succinic acid, hex-4-yn-3-yl propyl ester	-74.6	-87.7	-542.2	-76.2	-82.6	-85.7	-83.4
Q	Thiophene 3(1,1,-dimethylethyl)	-43.7	-61.4	-320.6	-45.6	-54.9	-54.0	-54.8
R	Thymine	-66.1	-74.9	-407.2	-38.0	-69.4	-66.4	-61.0

3.2. H – Bond profile for Dengue viruses protein with 18 ligands.

Table – 2: H – Bond profile for Dengue viral protein with 18 ligands

Ligand	Compound name	Envelope protein	NS1 protein	Trans membrane domain of NS2A	NS2B/NS3 protease	NS3 helicase	NS5 protein	Capsid protein
A	2,4-dihydroxy-2,5 dimethyl 3(2H),furan-3-one	H-M	-	-	H-M	H-S	H-M	H-S H-M
B	4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy 6 methyl	H-M	H-M H-S	-	-	H-S H-M	-	H-S
C	N,N,2,2-Tetramethylpropan-1-amine oxide	-	-	-	H-M	-	H-M	-
D	1,3,5 triazine 2,4,6 triamine	-	H-M H-S	H-M	-	-	-	H-S
E	2 chloro 1,3 benzenediol	H-M	-	H-M	-	H-S	H-M	H-S
F	2 flouro 5 methylaniline	-	H-M H-S	H-M	-	H-M	-	H-S
G	2 napthalenol	-	-	-	-	-	-	H-S H-M
H	2,4,5, triaminopyrimidine	-	-	H-M	-	-	-	H-S
I	2,6-piperazinedione, dioxime	-	-	H-M	-	H-M	H-M	H-M
J	3 Flouro benzyl alcohol	-	-	-	-	H-S	H-M	H-M H-S
K	4 flourobenzylalcohol	-	-	-	-	H-M		H-S
L	4,5-Diamino-2-hydroxypyrimidine	-	H-M H-S	-	-	-	H-M	H-M
M	10-Chlorodecyl (E) -2-methylbut-2-enoate	-	-	-	-	-	-	H-M
N	Butanoic acid 3-butenyl ester	-	-	-	H-M		H-M	H-S
O	Propanal, 2,3-dihydroxy-, (S)-	H-M	-	-	-	H-M	H-M	H-S
P	Succinic acid, hex-4-yn-3-yl propyl ester	-	-	-	-	-	-	H-M H-S
Q	Thiophene 3(1,1,-dimethylethyl)	-	-	-	-	-	-	H-M
R	Thymine	H-M	-	-	H-M	-	H-M	-

3.3. Amino acid position profile for Dengue viruses protein with 18 ligands.

Table – 3: Amino acid position profile for Dengue viral protein with 18 ligands

Ligand	Compound name	Envelope protein	NS1 protein	Trans membrane domain of NS2A	NS2B/NS3 protease	NS3 helicase	NS5 protein	Capsid protein
A	2,4-dihydroxy-2,5 dimethyl 3 (2H),furan-3-one	Ile (618)/ Arg (629)	-	-	Asp(58)	Asp(192)	Asp(254)	Arg(41) / Leu (44) / Lys(45)/ Leu(46)/ Phe(47)
B	4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy 6 methyl	Ile (618)/ Arg (629)	Ile(243)/ Thr 262)	-	-	Asp(192)/ Gly(462)	-	Arg(68)
C	N,N,2,2-Tetramethylpropan-1-amine oxide	-	-	-	Asp(58)	-	Gly(86)	-
D	1,3,5 triazine 2,4,6 triamine	-	Ile(243)/ Thr (262)	Leu(11)	-	-	-	Arg(68)/ Arg(41)
E	2 chloro 1,3 benzenediol	Ile (618)/ Arg (629)	-	Leu(11)	-	Asp(192)	Asp(254)	Arg(41)
F	2 flouro 5 methylaniline	-	Ile(243)/ Thr (262)	Leu(11)	-	Gly(462)	-	Arg(68)
G	2 napthalenol	-	-	-	-	-	-	Arg(41)/ Leu (44)/ Lys(45)/ Leu(46)/ Phe(47)
H	2,4,5, triaminopyrimidine	-	-	Leu(11)	-	-	-	Arg(41)
I	2,6-piperazinedione, dioxime	-	-	Leu(11)	-	Gly(462)	Cys(82)/Gly(86)/Trp(87)	Ala(49)
J	3 Flouro benzyl alcohol	-	-	-	-	Asp(192)	Asp(254)	Leu(29)/ Arg(68)
K	4 flourobenzylalcohol	-	-	-	-	Gly(462)	-	Arg(68)
L-	4,5-Diamino-2-hydroxypyrimidine	-	Ile(243)/ Thr (262)	-	-	-	Cys(82)/Gly(86)/Trp(87)	Leu(66)/ Lys(67)/ Gly(60)/ Arg(98)
M	10-Chlorodecyl (E) -2-methylbut-2-enoate	-	-	-	-	-	-	Leu(29)
N	Butanoic acid 3-butenyl ester	-	-	-	Asp(58)	-	Asp(254)	Arg(41)
O	Propanal, 2,3-dihydroxy-, (S)-	Ile (618)/ Arg (629)	-	-	-	Gly(462)	Cys(82)/Gly(86)/Trp(87)	Arg(49)
P	Succinic acid, hex-4-yn-3-yl propyl ester	-	-	-	-	-	-	Arg(22)/ Val(23)/ Ser(24)/ Thr(25)/ Thr(62)
Q	Thiophene 3(1,1,-dimethylethyl)	-	-	-	-	-	-	Leu(44)/ Lys(45)/ Leu(46)
R	Thymine	Ile (618)/ Arg (629)	-	-	Asp(58)	-	Cys(82)/Gly(86)/Trp(87)	-

4. DISCUSSION

From the Table – 1, Table – 2 and Table – 3, the 3D structure coordinates of seven non structural proteins of dengue virus is optimized and 18 compounds from Red *vitis vinifera* leaves extract are identified. Their total binding energy was calculated using iGEMDOCK. Evaluations of binding conformation of 18 compounds with seven non structural dengue viral proteins are performed using iGEMDOCK. From docking study, we listed binding affinity of 18 compounds based on ligand binding energy (Table.1). The binding pose for each ligand molecule into the non structural dengue viral protein is 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. Among the 18 analogs, compound I is found to have lower ligand binding energy (binding energy value= -75.39 kcal/mol), than other analogs for Envelope protein. Compound "P" has least binding energy score with NS1 protein (binding energy value= -87.7 kcal/mol), Trans membrane domain of NS2A (binding energy value= -542.22kcal/mol), NS2B / NS3 protease (binding energy value= -78.73kcal/mol), NS3 helicase (binding energy value= -88.5kcal/mol), NS5 protein (binding energy value= -86.53 kcal/mol) and Capsid protein (binding energy value = -83.46kcal/mol). We further analyzed the docked pose for finding the binding mode of compound "I" and compound "P" in to seven non structural dengue proteins to validate the reasonable binding conformations.

4.1. The Total Binding Energy for Dengue virus envelope protein with 18 ligands

From Table – 1, Table – 2, Table – 3 and Figure – 1, the docking simulation of 18 ligands were performed for Dengue virus envelope protein. From the docking study, we observed that compound – I has best binding affinity with the target envelope protein with the binding energy value of -75.89 kcal/mol. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus envelope protein with 18 ligands: is shown in Fig.1.

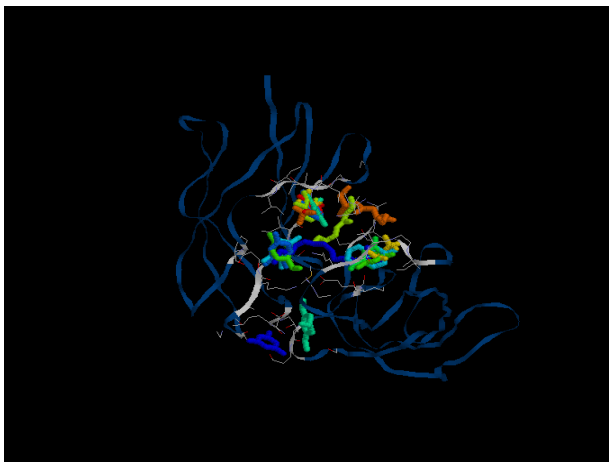

Fig.1: The Total Binding Energy for Dengue virus envelope protein with 18 ligands.

4.2. The Total Binding Energy for Dengue virus NS1 protein with 18 ligands

From Table – 1, Table – 2, Table – 3 and Figure – 2, the docking simulation of 18 ligands were performed for Dengue virus NS1 protein. From the docking study, we observed that compound – P has best binding affinity with the target NS1 protein with the binding energy value of -87.7 kcal/mol. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus NS1 protein with 18 ligands: is shown in Fig.2.

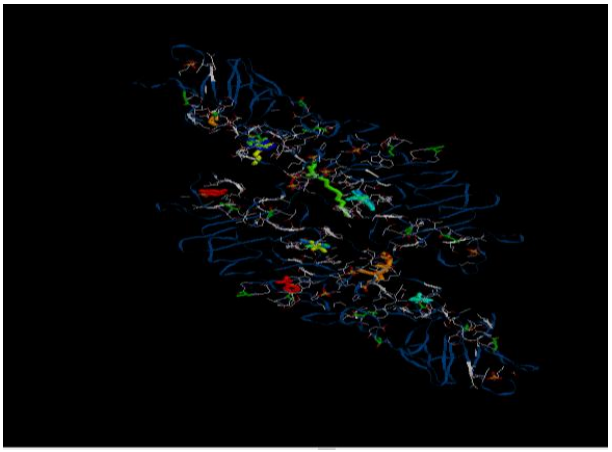

Fig.2: The Total Binding Energy for Dengue virus NS1 protein with 18 ligands.

4.3. The Total Binding Energy for Dengue virus Trans membrane domain of NS2A with 18 ligands

From Table – 1, Table – 2, Table – 3 and Figure – 3, the docking simulation of 5 ligands were performed for Dengue virus Trans membranedomain of NS2A. From the docking study, we observed that compound – P has best binding affinity with the target Trans membrane domain of NS2A with the binding energy value of -542.22 kcal/mol-. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus Trans membrane domain of NS2A with 18 ligands: is shown in Fig.3.

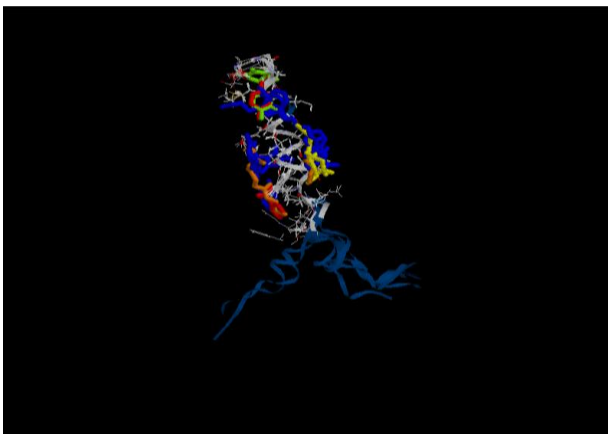

Fig.3: The Total Binding Energy for Dengue virus Trans membrane domain of NS2A with 18 ligands.

4.4. The Total Binding Energy for Dengue virus NS2B / NS3 protease with 18 ligands

From Table – 1, Table – 2, Table – 3 and Figure – 4, the docking simulation of 18 ligands were performed for Dengue virus NS2B / NS3protease. From the docking study, we observed that compound – I has best binding affinity with the target NS2B / NS3protease with the binding energy value of -78.73 kcal/mol. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus NS2B / NS3protease with 18 ligands: is shown in Fig.4.

Fig.4: The Total Binding Energy for Dengue virus NS2B / NS3 protease with 18 ligands.

4.5. The Total Binding Energy for Dengue virus NS3 helicase with 18 ligands

From Table – 1, Table – 2, Table – 3 and Figure – 5, the docking simulation of 18 ligands were performed for Dengue virus NS3 helicase**.**From the docking study, we observed that compound – I has best binding affinity with the target NS3 helicase with the binding energy value of -88.5 kcal/mol. A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus NS3 helicase with 18 ligands: is shown in Fig 5.

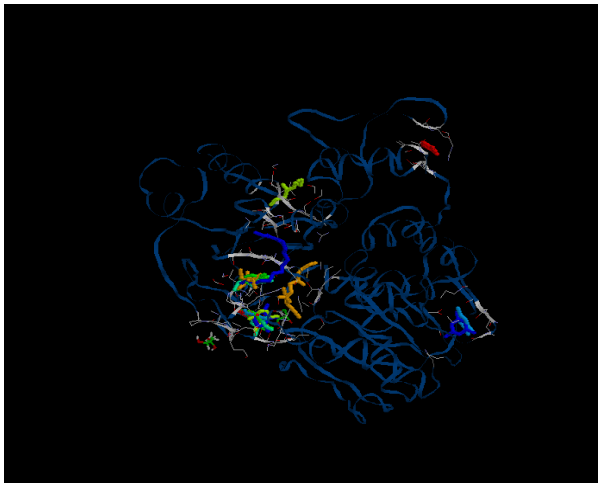

Fig.5: The Total Binding Energy for Dengue virus NS3 helicase with 18 ligands.

4.6. The Total Binding Energy for Dengue virus NS5 protein with 18 ligands

From Table – 1, Table – 2, Table – 3 and Figure – 6, the docking simulation of 18 ligands were performed for Dengue virus NS5 protein From the docking study, we observed that compound – I has best binding affinity with the target NS5 protein with the binding energy value of -86.53 kcal/mol. Interaction analysis of compound I in dengue virus NS5 reveals that it forms one hydrogen bond with low energy, with Cys(82), Gly(86), Trp(87) A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus NS5 protein with 18 ligands: is shown in Fig.6.

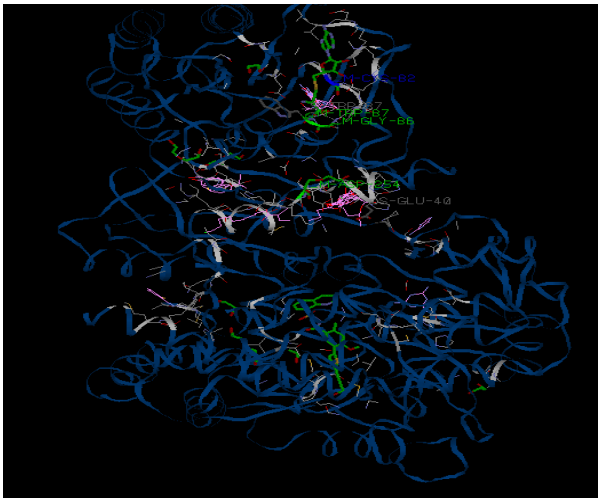

Fig.6: The Total Binding Energy for Dengue virus NS5 protein with 18 ligands.

4.7. The Total Binding Energy for Dengue virus Capsid protein with 18 ligands

From Table – 1, Table – 2, Table – 3 and Figure – 7, the docking simulation of 18 ligands were performed for Dengue virus Capsid protein. From the docking study, we observed that compound – P has best binding affinity with the target Capsid protein. with the binding energy value of -83.46 kcal/mol. Interaction analysis of binding mode of compound –P in dengue virus Capsid protein. reveals that it forms two hydrogen bonds with low energy, one with Arg(22) residue Val(23), Ser(24), Thr(25)and Thr(46). A close-up view of the Total Binding Energy (kcal/mol) profile for Dengue virus Capsid protein. with 18 ligands: is shown in Fig.7.

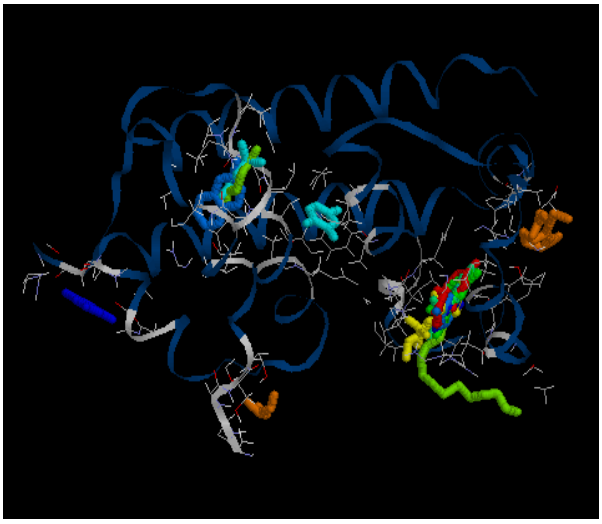

Fig.7: The Total Binding Energy for Dengue virus Capsid protein with 18 ligands.

5. CONCLUSION

Our molecular docking studies explored the possible binding modes of 18 compounds that are present in *Red Vitis vinifera* grape pulp extract with seven non structural proteins which are envelope protein, NS1 protein, Transmembrane domain of NS2A, NS2B/NS3 protease, NS3 helicase, NS5 protein and capsid protein. It revealed that all the 18 compounds show minimum affinity with all the proteins. Especially the compound I (2, 6-piperazinedione, dioxime) and compound P (Succinic acid, hex-4-yn-3-yl propyl ester) shows best results compared to other compounds. On comparing the binding energy and the binding site residues, we found that all compounds differ either in their binding modes or with the binding site residues for hydrogen bond formation. The conclusion drawn from our virtual screening and docking result was that the 2, 6-piperazinedione, dioxime and Succinic acid, hex-4-yn-3-yl propyl ester has highest binding affinity with most of the proteins and it can be used as an effective drug target for Dengue virus. However, validation of our results through *invivo* and *invitro* experiments along with animal models will enlighten hope for the future development of more potent drugs for the treating Dengue.

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