Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2015, 7(3):209-224

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

In silico screening of phytoactive components against Junin, Hanta, Dengue, Marburg and Ebola Viruses

Himani Badoni, *Sakshi Painuli and Prabhakar Semwal

Department of Biotechnology, Graphic Era University, 566/6, Bell Road, Clement Town, Dehradun, Uttarakhand, India

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ABSTRACT

Viruses are the most infectious agents which are found virtually in all life forms, like all other organisms, human race is also vulnerable to get infected by viruses. Viruses are potential in spreading catastrophic epidemics through their pathogenicity to the entire human race. Researchers nowadays are afraid of a major outbreak of baneful and indocile viral diseases which can spread through different modes. In this article, we had selected five such dreadful viruses; Junin, Hanta, Dengue, Marburg and Ebola along with 50 known bioactive components under our study. This study is an effort in discovering effective bioactive components from the list of selected bioactive components to inhibit the activity against these viruses by means of in silico analysis. Molecular docking studies were performed using iGEMDOCK module software. All the selected components from the list were docked with the specific protein binding sites of the viruses. According to the iGEMDOCK software palmatine (-103.076 kcal/mol), delphinidin chloride (-109.187 kcal/mol), squalene (-109.975 kcal/mol) and marmin (-91.84 kcal/mol, 98.74 kcal/mol) shows highest binding energy, whereas d-limonene and allicin shows minimum binding energy against binding sites. Further in vitro and in vivo analysis of these compounds against these protein viruses will lead a new pathway to drug discovery.

Keywords: Junin, Hanta, Dengue, Marburg, Ebola, bioactive compounds, *in silico*

INTRODUCTION

A virus is a small infectious agent that posses some, but not all qualities of living organism. They are said to be "Organism at the edge of life". Viruses are capable to infect all types of life forms, from fauna and flora to micro organism [1]. They are found in almost every ecosystem on Earth and are said to be most abundant type of biological entity [2, 3]. Spreading of virus can be of many ways, viruses affecting plants spread through plant and some insects. Viruses in animals can be carried by bloodsucking insects or through animals which acts as vectors. Virus particles are composed of three main important parts of their existence, one is genetic material another is protein coats for its protection and at last is enveloped for protecting protein outside the in unfavorable condition. Viruses can exist in different shapes ranging from simple to icosahedral or more complex. Virulence is the property of the virus to cause disease and most virus diseases cause death of the host organism. In history there is an evidence for number of epidemics and pandemics caused due to viral outbreaks. Our world had lost millions of lives due to viral epidemics. To suppress the activity of virus infection our body builds up an immune response that usually eliminates the infecting virus. But not every time our immune system figures out the immune response against viruses. Sometimes viruses may play more playful plots against our immunity and outbreak the resistant wall and cause baneful disease.

To antagonize this problem several vaccines had been developed against a range of viruses. Merely some viruses are so potent that there is no effectual vaccine yet developed against them. Hence there is a need for new drugs and approaches to fight the aliveness threatened by several vaccines and computer aided drug design is one of the mighty tools for attaining novel drugs which protein target or gene targets of pathogenic viruses. There are several viruses which can cause harm in a prominent way. For *in silico* study of the potency of selected phytoconstituents, we have selected five deathly viruses via Hanta, Junin, Dengue, Marburg and Ebola virus.

Hanta virus belongs to Bunyaviridae family, its name is derived from the Hanta river of South Korea, the region said to be affected first. The virus is enveloped and contains negative sense, single-stranded RNA. Hanta virus produces fatal disease in human such as Hanta virus hemorrhagic fever with renal syndrome (HFRS) and Hanta virus pulmonary syndrome (HPS). The vectors for Hanta virus are rodents. Till now there are more than 20 identified strains of the Hanta virus. However, no Hanta virus vaccine has been approved for purpose in the US and no vaccine won the widespread acceptance. The work for developing effective and safe vaccine is still going on [3]. Another deathly virus on the list is Junin virus, which belongs to Arenaviridae family. It causes Argentine hemorrhagic fever (AHF), it is spread through rodents. Candid 1 vaccine was developed against it by US Army medical research institute. Next virus to target is dengue virus. It belongs to Flaviviridae family and is mosquito-borne viral disease. According to World Health Organization (WHO) "Over 2.5 billion people-over 40% of the world's population are now at risk from dengue". It is disseminated by the *Aedes aegypti mosquito*, a female mosquito, which when bites and infected human become carrier for Dengue virus and serve as virus reservoir to uninfected humans. In India, total drug market affected by this disease, approximately 27.4 million USD economic burdens faced by Dengue [4]. Till date, there is no specific treatment present for Dengue/severe Dengue; it can be treated in the early stages [5].

Marburg virus is also a deadly virus which belongs to Filoviridae family and its name was derived from Marburg city (Germany). It contains single - stranded RNA genome. Marburg virus causes fatal disease in human and non human primates and cause viral hemorrhagic fever. It is transmitted by direct contact with the blood, body fluids and tissues of infected persons and dead infected wild animals, however no vaccines have been yet approved for use. Last virus from our list is from the same family i.e. Filoviridae family and it is Ebola virus. Ebola and Marburg are closely related viruses; Ebola virus creates severe and even fatal illness in humans. It was first discovered in 1976 in South Africa near Ebola river [6]. It is transmitted through the same route as mentioned for Marburg virus. It causes hemorrhagic fever to infected body; this virus does not spread through air, water or food. There is no yet authorized vaccine or medication for Ebola and Marburg [7].

In this paper we tried to target the selected viruses from "chosen bioactive components". The confront investigation conducts the binding of selected protein sites which play an important part in ruling the pathogenicity of these viruses with herbal bioactive compounds. Now a day's computer aided drug designing play a very important role in the selection of effective drug or combination of two or more drugs. It is a potent tool for introducing novel drugs against specific targets. The technique is molecular docking and it is a vital tool in structural molecular biology and computer aided drug designing. For the prophecy of binding affinity of protein and compound scoring function is used. We had used *i*Gemdock, a structure-based virtual screening framework out of the many docking programs available. The docking and screening tool of *i*Gemdock is Gemdock which is studied for virtual screening and post screening analysis. It also provides visualization of the protein-compound interaction profiles of hydrogen-bonding (H), Vander Waals (V) interaction and electrostatic force (E) and along with that it also depicts the hierarchical clustering dendogram of compounds which are needed for post-screening analysis [8,9]. However, other experimental studies via *in vitro* and *in vivo* are required to confirm.

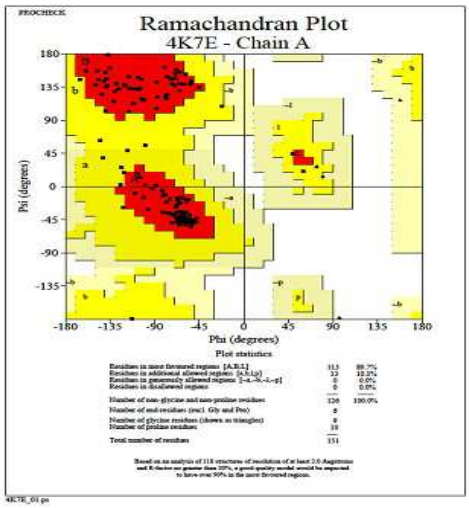
EXPERIMENTAL SECTION

Protein of concern

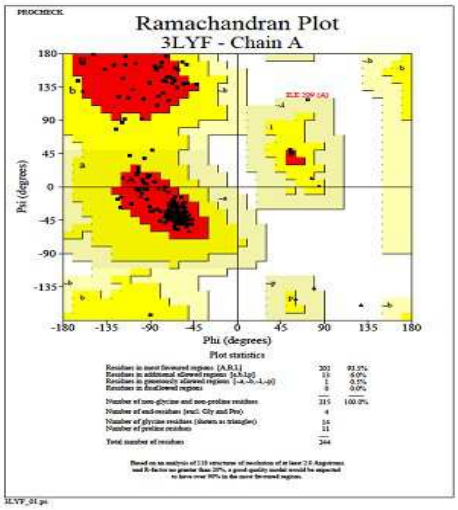
The crystal structures of protein for the selected viruses were downloaded as PDB files from RSCB protein data bank and they all were then evaluated through Ramachandran plot examined via PROCHECK from EBI server to inspect the superiority of the target protein structure.

S. No.	Virus Name	Protein PDB- ID
1	Junin virus	PDBID-4K7E
2	Hanta virus	PDBID-3LYF
3	Dengue virus	PDBID-3L6P
4	Marburg virus	PDBID-4GH9
5	Ebola virus	PDBID-218B

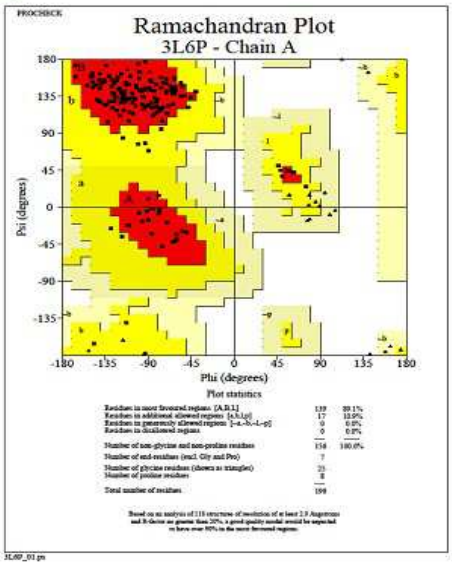
(A)



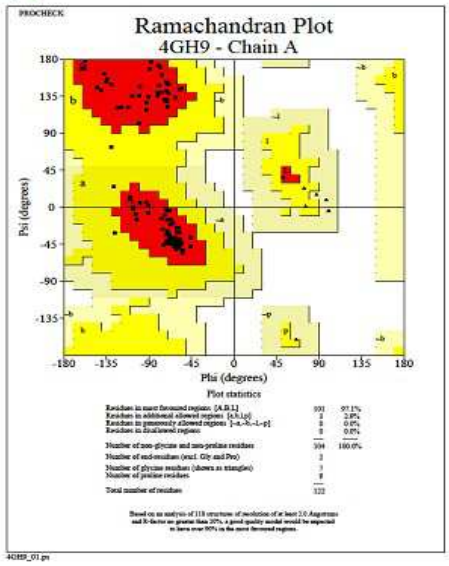
(B)



(C)



(D)



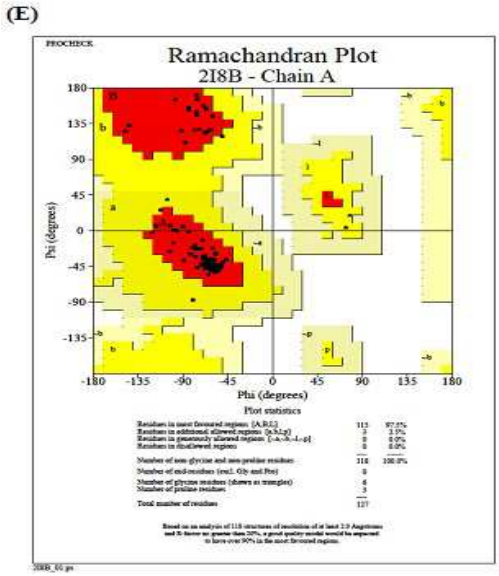
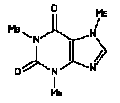
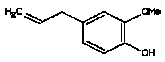
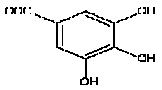
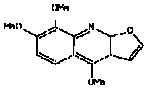
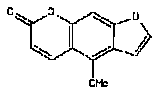
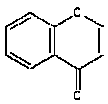
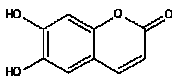


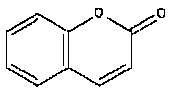
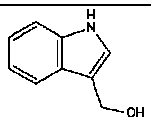
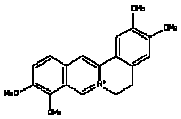
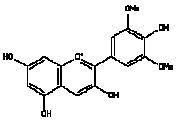
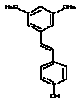
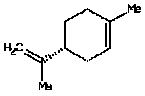
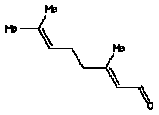
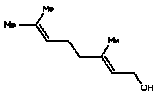
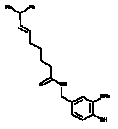
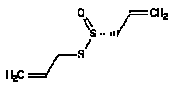
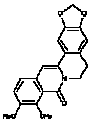
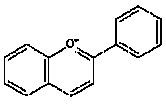
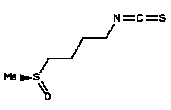
Figure 1: Ramachandran plots as showing the stability of all predicted model (targeted proteins) (A) Junin virus (B) Hanta virus (C) Dengue virus (D) Marburg virus and (E) Ebola virus, which are generated by PROCHECK software

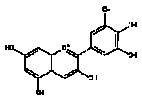
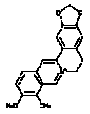
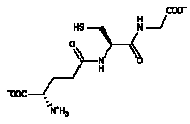
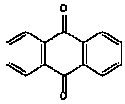
Ligand molecules chosen for docking

A total of 50 bioactive compounds were isolated from high altitude medicinal plants and selected for study on the basis of previous literature. Structures of all the bioactive compounds were downloaded from ZINC AC in MOL-2 format (Chemical structure and Zinc id of all 50 components are in table 1).

Table 1: All 50 phytoactive components with chemical structure and zinc id (Adapted from Zinc AC data base)

S.N.	Components name	Zinc id	Structure
1.	Caffeine	zinc_1084	
2.	Eugenol	zinc_1411	
3.	Gallic acid	zinc_1504	
4.	Skimmianine	zinc_35525	
5.	Bergapten	zinc_57731	
6.	Chromone	zinc_57736	
7.	Esculetin	zinc_57908	

8.	Coumarin	zinc_74709	
9.	Indole-3-carbinol	zinc_158743	
10.	Palmatine	zinc_608233	
11.	Malvidin	zinc_897714	
12.	Pterostilbene	zinc_899213	
13.	d-Limonene	zinc_967513	
14.	Citral	zinc_1529208	
15.	Geraniol	zinc_1529210	
16.	Capsaicin	zinc_1530575	
17.	Allicin	zinc_1530846	
18.	Berlambine	zinc_1604019	
19.	Flavylium	zinc_1670024	
20.	Sulforaphane	zinc_2557133	

21.	Delphinidin chloride	zinc_3777403	
22.	Berberine chloride	zinc_3779067	
23.	Glutathione	zinc_3830891	
24.	Anthraquinone	zinc_3847491	
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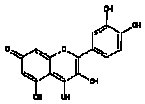
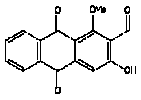
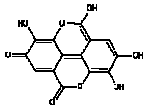
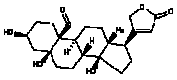
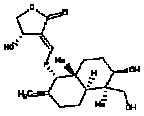
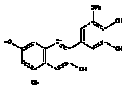
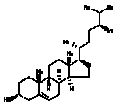
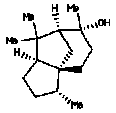
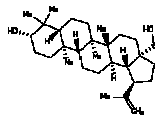
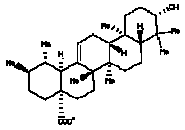
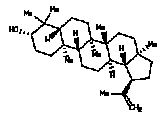
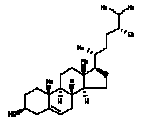
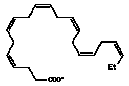
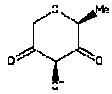
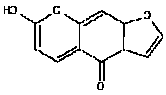
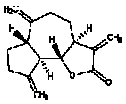
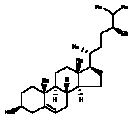
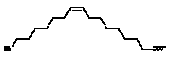
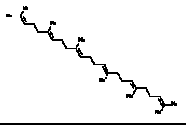
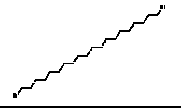
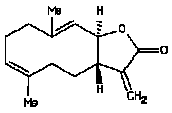
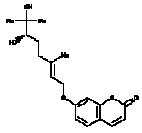
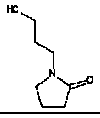
26.	Quercetin	zinc_3869685	
27.	Damnacanthal	zinc_3872206	
28.	Ellagic acid	zinc_3872446	
29.	Strophanthidin	zinc_3875425	
30.	Andrographolide	zinc_3881796	
31.	Petunidin	zinc_3954302	
32.	beta-Sitosterol	zinc_3978429	
33.	Cedrol	zinc_3978625	

34.	Betulin	zinc_3978650	
35.	Ursolic acid	zinc_3978827	
36.	Lupeol	zinc_4081455	
37.	beta-Sitosterol	zinc_4095717	
38.	Docosahexaenoic Acid	zinc_4474564	
39.	Methyl linoleate	zinc_4501378	
40.	3,5-dihydroxy-6-methyl-2H-pyran-4(3H)-one	zinc_5766182	
41.	Bergaptol	zinc_5842977	
42.	Palmitic acid	zinc_6072466	
43.	Dehydrocostus lactone	zinc_6361655	
44.	Phytosterol	zinc_6393492	
45.	Oleic acid	zinc_6845860	
46.	Squalene	zinc_6845904	

47.	Docosanol	zinc_6920384	
48.	Costunolide	zinc_13585362	
49.	Marmin	zinc_14587259	
50.	1-(3-Hydroxypropyl)-2-pyrrolidone	zinc_14806511	

Molecular Docking

For docking *i*Gemdock software is employed, in *i*Gemdock application first we have to select the ligand or several ligands at a time and then protein binding site. Virtual screening procedure of *i*Gemdock consists of four main steps; target protein preparation, compound library, docking and post-screening analysis [9]. After docking is accomplished the software generates protein-compound interaction profile and ranks the compounds according their pharmacological energies. The pharmacological scoring depends on dock energy of GEMDOCK, pharma scores of electrostatic force, hydrogen bond and Vander Waals interaction. The binding energy depicts how well a ligand binds to the target protein and the software also yields the image for visualization of pharmacological interactions [10]. .

RESULTS AND DISCUSSION

The overall objective of this work was to select the best suited bioactive compound which can get docked with selected virus protein from the list of 50 bioactive compounds. The docking was performed with the help of *i*GEMDOCK by calculating their binding energy in the form of Vander Waals energy, electrostatic energy and hydrogen bonding. *i*GEMDOCK is a tool which can allow a better and starting point for deducing pharmacological interaction which further results in distinguishing a new novel and potentially active compounds for a specific protein, responsible for causing diseases. The hierarchical clustering dendogram [Fig. 2 (A, B, C, D and E)] shows the post screening analysis module. The summary of docking results between targeted proteins and phytocomponents was shown in table 2, 3, 4, 5 and 6. The highest binding energy of receptor - ligand interactions supports the fitting of the drug to the target molecules. It can be calculated that according to *i*GEMDOCK palmatine, delphinidine, squalene and marmine showed best binding results in 4K7E, 3LYF, 3L6P, 4GH9 and 218B [Fig. 3 (A, B, C, D and E)] proteins of Junin, Hanta, Dengue, Marburg and Ebola virus. Lesser the energy, the greater will be accepted of the chemical as a drug. Thus study reports that the compounds having highest binding energy are very effective in halting the undesirable effects of selected viruses and these bioactive compounds can be further used for analyzing *in vivo* potency of these bioactive compounds in the case of these viruses.

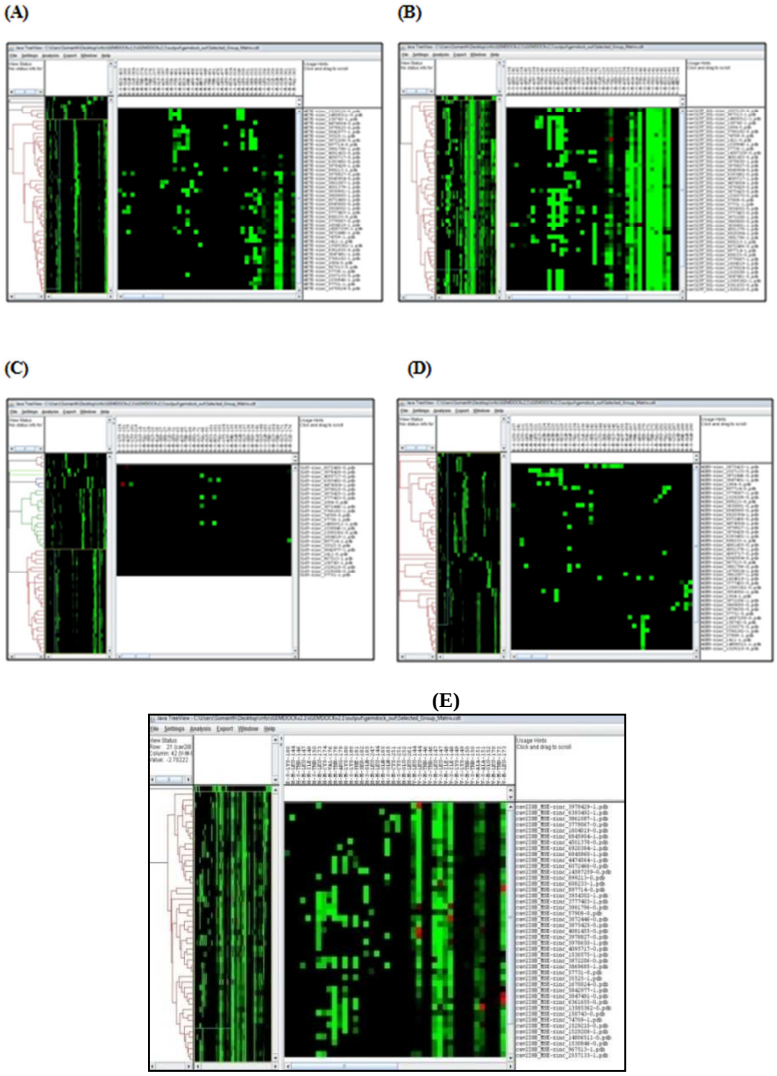


Figure 2: Figure 2 indicates the hierarchical clustering dendogram for (A) Junin virus (B) Hanta virus (C) Dengue virus (D) Marburg virus and (E) Ebola virus, show the post screening analysis module

Table 2: Results of docking between different ligands and targeted protein in the form of total binding energy for Junin virus

SN	Compound	Energy	VDW	H Bond	Elec
1.	**4K7E-zinc_608233-0.pdb**	**-103.076**	**-103.076**	**0**	**0**
2.	4K7E-zinc_14587259-1.pdb	-100.804	-88.2386	-12.5654	0
3.	4K7E-zinc_897714-0.pdb	-100.639	-83.4935	-17.1458	0
4.	4K7E-zinc_3777403-1.pdb	-98.6098	-86.1966	-12.4132	0
5.	4K7E-zinc_3869685-1.pdb	-97.5321	-79.8375	-17.6946	0
6.	4K7E-zinc_3881796-1.pdb	-96.7628	-76.1447	-20.6181	0
7.	4K7E-zinc_3779067-0.pdb	-96.6483	-94.7391	-1.90919	0
8.	4K7E-zinc_3954302-1.pdb	-95.4493	-84.2979	-11.1514	0
9.	4K7E-zinc_3861087-1.pdb	-95.0991	-84.3404	-10.7587	0
10.	4K7E-zinc_3872446-1.pdb	-95.0666	-76.8956	-18.171	0
11.	4K7E-zinc_1604019-1.pdb	-94.7577	-91.4867	-3.27099	0
12.	4K7E-zinc_6845904-0.pdb	-93.0099	-93.0099	0	0
13.	4K7E-zinc_3978650-1.pdb	-91.8426	-82.4612	-9.38142	0
14.	4K7E-zinc_3830891-1.pdb	-91.5396	-68.0859	-21.8597	-1.59399
15.	4K7E-zinc_4095717-0.pdb	-91.2038	-88.7038	-2.5	0
16.	4K7E-zinc_3978429-1.pdb	-89.9037	-86.4037	-3.5	0
17.	4K7E-zinc_3872206-0.pdb	-89.7377	-76.7377	-13	0
18.	4K7E-zinc_35525-1.pdb	-89.4069	-76.3915	-13.0154	0
19.	4K7E-zinc_1530575-0.pdb	-88.589	-70.7223	-17.8667	0
20.	4K7E-zinc_3875425-1.pdb	-86.6715	-63.2054	-23.4661	0
21.	4K7E-zinc_6393492-0.pdb	-85.9012	-83.4012	-2.5	0
22.	4K7E-zinc_899213-1.pdb	-85.8246	-76.4664	-9.35824	0
23.	4K7E-zinc_6920384-1.pdb	-83.674	-77.7002	-5.97378	0
24.	4K7E-zinc_3978827-0.pdb	-82.9403	-75.6933	-7.24696	0
25.	4K7E-zinc_6845860-0.pdb	-82.3679	-79.0137	-3.35425	0
26.	4K7E-zinc_5842977-1.pdb	-80.7692	-60.8033	-19.9659	0
27.	4K7E-zinc_4081455-0.pdb	-78.9964	-76.4964	-2.5	0
28.	4K7E-zinc_1670024-0.pdb	-78.6948	-75.1948	-3.5	0
29.	4K7E-zinc_6072466-1.pdb	-78.4571	-73.4096	-5.04753	0
30.	4K7E-zinc_4474564-0.pdb	-77.5369	-70.8617	-6.67517	0
31.	4K7E-zinc_4501378-1.pdb	-77.088	-63.7858	-13.3022	0
32.	4K7E-zinc_3847491-1.pdb	-74.8639	-71.3639	-3.5	0
33.	4K7E-zinc_57731-1.pdb	-74.5465	-69.7611	-4.78542	0
34.	4K7E-zinc_6361655-0.pdb	-69.9365	-65.0875	-4.84897	0
35.	4K7E-zinc_1084-0.pdb	-69.8563	-60.1453	-9.71095	0
36.	4K7E-zinc_13585362-1.pdb	-69.8306	-66.3762	-3.45437	0
37.	4K7E-zinc_57908-1.pdb	-66.2146	-45.2528	-20.9618	0
38.	4K7E-zinc_1504-1.pdb	-65.5478	-46.5732	-18.9746	0
39.	4K7E-zinc_158743-1.pdb	-64.5017	-43.1433	-21.3584	0
40.	4K7E-zinc_3978625-0.pdb	-62.0425	-55.6884	-6.35415	0
41.	4K7E-zinc_1411-1.pdb	-61.1266	-49.1266	-12	0
42.	4K7E-zinc_5766182-1.pdb	-61.0302	-49.3235	-11.7067	0
43.	4K7E-zinc_1529210-0.pdb	-60.9937	-46.3445	-14.6492	0
44.	4K7E-zinc_57736-1.pdb	-60.0027	-57.5182	-2.48447	0
45.	4K7E-zinc_74709-1.pdb	-59.6884	-51.0744	-8.61398	0
46.	4K7E-zinc_14806511-0.pdb	-58.5342	-38.7645	-19.7697	0
47.	4K7E-zinc_1529208-1.pdb	-58.285	-55.785	-2.5	0
48.	4K7E-zinc_2557133-0.pdb	-51.3285	-46.186	-5.14254	0
49.	4K7E-zinc_1530846-1.pdb	-50.0909	-44.2848	-5.80612	0
50.	4K7E-zinc_967513-0.pdb	-49.9425	-49.9425	0	0

Table 3: Results of docking between different ligands and targeted protein in the form of total binding energy for Hanta virus

SN	Compound	Energy	VDW	HBond	Elec
1.	**3LYF_zinc_3777403-0.pdb**	**-109.187**	**-79.7387**	**-29.448**	**0**
2.	3LYF_zinc_3869685-0.pdb	-106.678	-83.3998	-23.2784	0
3.	3LYF_zinc_3875425-0.pdb	-106.144	-74.8889	-31.2552	0
4.	3LYF_zinc_3978827-0.pdb	-103.192	-90.9092	-10.2875	-1.99552
5.	3LYF_zinc_3954302-0.pdb	-101.967	-74.1297	-27.8372	0
6.	3LYF_zinc_897714-1.pdb	-101.497	-80.9183	-20.5791	0
7.	3LYF_zinc_3978650-1.pdb	-100.196	-87.2338	-12.9625	0
8.	3LYF_zinc_3881796-1.pdb	-100.042	-70.6375	-29.4045	0
9.	3LYF_zinc_14587259-0.pdb	-97.8974	-82.3288	-15.5686	0
10.	3LYF_zinc_3779067-1.pdb	-96.481	-86.9846	-9.49642	0
11.	3LYF_zinc_1604019-1.pdb	-95.9345	-87.4658	-8.46871	0
12.	3LYF_zinc_4095717-1.pdb	-95.5254	-87.9867	-7.5387	0
13.	3LYF_zinc_6393492-0.pdb	-95.371	-88.4798	-6.89121	0
14.	3LYF_zinc_3872206-1.pdb	-95.0924	-78.6668	-16.4256	0
15.	3LYF_zinc_3830891-1.pdb	-94.4141	-57.3939	-31.5	-5.52016
16.	3LYF_zinc_3872446-0.pdb	-94.4117	-46.101	-48.3107	0
17.	3LYF_zinc_608233-0.pdb	-93.4806	-79.4771	-14.0035	0
18.	3LYF_zinc_4081455-0.pdb	-91.7321	-85.7321	-6	0
19.	3LYF_zinc_3978429-0.pdb	-89.6376	-84.6376	-5	0
20.	3LYF_zinc_899213-1.pdb	-89.5971	-68.3027	-21.2944	0
21.	3LYF_zinc_6845860-0.pdb	-88.0783	-72.0048	-13.8608	-2.21269
22.	3LYF_zinc_6845904-0.pdb	-87.2654	-87.2654	0	0
23.	3LYF_zinc_1530575-0.pdb	-86.027	-72.7651	-13.2619	0
24.	3LYF_zinc_6920384-1.pdb	-84.8767	-73.3098	-11.5669	0
25.	3LYF_zinc_4474564-1.pdb	-84.4705	-79.4705	-5	0
26.	3LYF_zinc_35525-0.pdb	-83.8364	-62.4809	-21.3555	0
27.	3LYF_zinc_3861087-0.pdb	-82.9856	-72.4856	-10.5	0
28.	3LYF_zinc_6361655-0.pdb	-82.1838	-69.864	-12.3198	0
29.	3LYF_zinc_13585362-1.pdb	-80.4271	-62.6615	-17.7656	0
30.	3LYF_zinc_6072466-0.pdb	-80.3819	-63.7959	-13.8877	-2.69826
31.	3LYF_zinc_5842977-0.pdb	-79.4878	-55.0399	-24.4479	0
32.	3LYF_zinc_4501378-1.pdb	-79.2776	-66.4074	-12.8702	0
33.	3LYF_zinc_3847491-0.pdb	-78.1054	-67.7367	-10.3687	0
34.	3LYF_zinc_57731-1.pdb	-77.867	-57.031	-20.836	0
35.	3LYF_zinc_1504-1.pdb	-73.455	-44.1735	-26.541	-2.74046
36.	3LYF_zinc_57908-0.pdb	-70.2135	-51.1755	-19.038	0
37.	3LYF_zinc_1670024-0.pdb	-70.1014	-70.1014	0	0
38.	3LYF_zinc_1411-0.pdb	-69.1974	-52.9951	-16.2023	0
39.	3LYF_zinc_1084-0.pdb	-68.7429	-51.2954	-17.4475	0
40.	3LYF_zinc_158743-1.pdb	-66.048	-49.2665	-16.7815	0
41.	3LYF_zinc_3978625-0.pdb	-64.2687	-53.7687	-10.5	0
42.	3LYF_zinc_14806511-1.pdb	-63.6731	-42.9558	-20.7173	0
43.	3LYF_zinc_74709-0.pdb	-61.5788	-48.4643	-13.1145	0
44.	3LYF_zinc_57736-1.pdb	-61.4328	-50.9328	-10.5	0
45.	3LYF_zinc_1529208-1.pdb	-60.5176	-50.0178	-10.4998	0
46.	3LYF_zinc_5766182-0.pdb	-59.9595	-43.5023	-16.4572	0
47.	3LYF_zinc_1529210-0.pdb	-59.2568	-48.7568	-10.5	0
48.	3LYF_zinc_2557133-0.pdb	-59.1413	-41.8016	-17.3397	0
49.	3LYF_zinc_1530846-1.pdb	-52.2293	-41.7293	-10.5	0
50.	3LYF_zinc_967513-1.pdb	-47.5645	-47.5645	0	0

Table 4: Results of docking between different ligands and targeted protein in the form of total binding energy for Dengue

SN	Compound	Energy	VDW	HBond	Elec
1.	**3L6P-zinc_6845904-1.pdb**	**-109.975**	**-109.975**	**0**	**0**
2.	3L6P-zinc_897714-1.pdb	-107.966	-74.0126	-33.9532	0
3.	3L6P-zinc_3830891-1.pdb	-104.73	-75.1122	-28.8944	-0.723734
4.	3L6P-zinc_3954302-1.pdb	-102.155	-85.4122	-16.7425	0
5.	3L6P-zinc_3777403-0.pdb	-100.727	-73.3014	-27.4253	0
6.	3L6P-zinc_3881796-1.pdb	-98.3785	-80.0338	-18.3447	0
7.	3L6P-zinc_1604019-1.pdb	-96.3379	-76.9154	-19.4225	0
8.	3L6P-zinc_14587259-1.pdb	-95.9709	-84.0066	-11.9643	0
9.	3L6P-zinc_3875425-1.pdb	-93.9053	-77.2744	-16.6309	0
10.	3L6P-zinc_3861087-0.pdb	-93.3188	-88.3188	-5	0
11.	3L6P-zinc_3869685-1.pdb	-93.2371	-71.8725	-21.3646	0
12.	3L6P-zinc_3978650-1.pdb	-92.3163	-85.9633	-6.35303	0
13.	3L6P-zinc_899213-1.pdb	-91.9556	-86.7063	-5.24925	0
14.	3L6P-zinc_35525-0.pdb	-91.6471	-72.0076	-19.6395	0
15.	3L6P-zinc_3978429-0.pdb	-90.8631	-82.2185	-8.64461	0
16.	3L6P-zinc_3872446-1.pdb	-90.558	-59.8988	-30.6592	0
17.	3L6P-zinc_6393492-0.pdb	-89.2169	-84.9297	-4.28724	0
18.	3L6P-zinc_3978827-1.pdb	-88.6748	-81.834	-6	-0.840781
19.	3L6P-zinc_4474564-1.pdb	-87.6791	-78.2426	-9.18229	-0.254219
20.	3L6P-zinc_1530575-1.pdb	-87.4904	-70.3483	-17.1421	0
21.	3L6P-zinc_4095717-0.pdb	-86.553	-84.053	-2.5	0
22.	3L6P-zinc_6920384-1.pdb	-85.9044	-83.7489	-2.15552	0
23.	3L6P-zinc_608233-0.pdb	-84.9128	-80.5312	-4.38158	0
24.	3L6P-zinc_5842977-1.pdb	-84.0096	-61.5365	-22.4731	0
25.	3L6P-zinc_3779067-0.pdb	-83.9563	-81.7849	-2.17136	0
26.	3L6P-zinc_3872206-0.pdb	-82.4625	-68.1499	-14.3126	0
27.	3L6P-zinc_4501378-1.pdb	-82.3779	-77.445	-4.93286	0
28.	3L6P-zinc_4081455-1.pdb	-80.9909	-74.9909	-6	0
29.	3L6P-zinc_6072466-0.pdb	-78.9344	-71.4148	-8.02113	0.501572
30.	3L6P-zinc_57731-1.pdb	-78.2697	-64.3564	-13.9133	0
31.	3L6P-zinc_1504-1.pdb	-78.2391	-45.2931	-32.946	0
32.	3L6P-zinc_6361655-1.pdb	-76.5707	-67.191	-9.37968	0
33.	3L6P-zinc_13585362-0.pdb	-75.8918	-65.536	-10.3558	0
34.	3L6P-zinc_3847491-1.pdb	-74.9944	-68.9944	-6	0
35.	3L6P-zinc_57908-1.pdb	-74.2143	-55.203	-19.0113	0
36.	3L6P-zinc_6845860-0.pdb	-73.6165	-70.2934	-3.32312	0
37.	3L6P-zinc_1670024-1.pdb	-70.7609	-67.2723	-3.48858	0
38.	3L6P-zinc_158743-1.pdb	-70.2948	-50.4375	-19.8573	0
39.	3L6P-zinc_1084-0.pdb	-70.0683	-50.822	-19.2463	0
40.	3L6P-zinc_1411-0.pdb	-68.6456	-57.6456	-11	0
41.	3L6P-zinc_1529208-0.pdb	-65.484	-54.984	-10.5	0
42.	3L6P-zinc_14806511-1.pdb	-64.3948	-48.1651	-16.2297	0
43.	3L6P-zinc_74709-0.pdb	-64.0189	-45.527	-18.4919	0
44.	3L6P-zinc_5766182-1.pdb	-63.4517	-37.735	-25.7167	0
45.	3L6P-zinc_3978625-0.pdb	-63.2705	-51.2787	-11.9918	0
46.	3L6P-zinc_1529210-0.pdb	-62.4284	-53.5336	-8.89477	0
47.	3L6P-zinc_57736-1.pdb	-60.037	-49.537	-10.5	0
48.	3L6P-zinc_2557133-0.pdb	-58.1377	-48.6377	-9.5	0
49.	3L6P-zinc_1530846-1.pdb	-55.3676	-44.9261	-10.4415	0
50.	3L6P-zinc_967513-1.pdb	-51.6224	-51.6224	0	0

Table 5: Results of docking between different ligands and targeted protein in the form of total binding energy for Marburg virus

SN	Compound	Energy	VDW	HBond	Elec
1.	**4GH9-zinc_14587259-0.pdb**	**-91.847**	**-70.9375**	**-20.9095**	**0**
2.	4GH9-zinc_1604019-1.pdb	-89.8873	-73.625	-16.2623	0
3.	4GH9-zinc_6845904-0.pdb	-88.679	-88.679	0	0
4.	4GH9-zinc_3954302-1.pdb	-86.1914	-62.1914	-24	0
5.	4GH9-zinc_3978827-1.pdb	-84.6269	-74.4117	-10.2152	0
6.	4GH9-zinc_608233-1.pdb	-82.3532	-80.1455	-2.20766	0
7.	4GH9-zinc_3830891-0.pdb	-81.7511	-67.4761	-13	-1.275
8.	4GH9-zinc_6845860-0.pdb	-80.7809	-78.736	-1.79337	-0.251485
9.	4GH9-zinc_897714-0.pdb	-80.5604	-61.6215	-18.9389	0
10.	4GH9-zinc_4474564-1.pdb	-80.5375	-79.3202	-1.21729	0
11.	4GH9-zinc_6920384-1.pdb	-80.2579	-77.7579	-2.5	0
12.	4GH9-zinc_3869685-0.pdb	-78.9627	-55.4133	-23.5494	0
13.	4GH9-zinc_4095717-0.pdb	-78.1395	-75.6395	-2.5	0
14.	4GH9-zinc_3872446-0.pdb	-77.6249	-54.1411	-23.4838	0
15.	4GH9-zinc_899213-0.pdb	-77.311	-75.297	-2.01403	0
16.	4GH9-zinc_1530575-0.pdb	-76.9508	-58.3909	-18.5599	0
17.	4GH9-zinc_3875425-1.pdb	-76.8215	-54.4294	-22.3921	0
18.	4GH9-zinc_3861087-1.pdb	-76.6534	-73.1534	-3.5	0
19.	4GH9-zinc_3978650-0.pdb	-76.1614	-59.2872	-16.8742	0
20.	4GH9-zinc_3777403-0.pdb	-75.6874	-57.9141	-17.7733	0
21.	4GH9-zinc_3779067-1.pdb	-75.4069	-66.8078	-8.5991	0
22.	4GH9-zinc_3881796-0.pdb	-75.2517	-64.7517	-10.5	0
23.	4GH9-zinc_4501378-1.pdb	-74.6581	-71.1581	-3.5	0
24.	4GH9-zinc_6072466-0.pdb	-74.5185	-72.0185	-2.5	0
25.	4GH9-zinc_4081455-0.pdb	-73.9506	-71.4506	-2.5	0
26.	4GH9-zinc_6393492-1.pdb	-73.5976	-73.5976	0	0
27.	4GH9-zinc_3978429-0.pdb	-73.585	-71.9406	-1.64442	0
28.	4GH9-zinc_3872206-1.pdb	-73.0923	-62.2153	-10.877	0
29.	4GH9-zinc_35525-0.pdb	-71.1986	-58.296	-12.9026	0
30.	4GH9-zinc_1670024-1.pdb	-66.6088	-63.1088	-3.5	0
31.	4GH9-zinc_1411-1.pdb	-64.2581	-48.407	-15.8511	0
32.	4GH9-zinc_57908-1.pdb	-63.0969	-45.0592	-18.0377	0
33.	4GH9-zinc_5842977-1.pdb	-62.3631	-54.7624	-7.60073	0
34.	4GH9-zinc_57731-0.pdb	-62.0788	-45.2507	-16.8281	0
35.	4GH9-zinc_1504-1.pdb	-61.2428	-38.2328	-23.01	0
36.	4GH9-zinc_158743-0.pdb	-60.1285	-41.431	-18.6975	0
37.	4GH9-zinc_3847491-1.pdb	-58.534	-55.034	-3.5	0
38.	4GH9-zinc_6361655-1.pdb	-58.5174	-58.5174	0	0
39.	4GH9-zinc_1084-0.pdb	-58.4323	-49.0594	-9.37292	0
40.	4GH9-zinc_13585362-0.pdb	-57.7311	-44.7568	-12.9743	0
41.	4GH9-zinc_74709-0.pdb	-56.2403	-48.2882	-7.95211	0
42.	4GH9-zinc_2557133-0.pdb	-55.4697	-37.8557	-17.614	0
43.	4GH9-zinc_5766182-1.pdb	-55.3483	-36.7242	-18.6241	0
44.	4GH9-zinc_14806511-1.pdb	-54.6413	-47.6879	-6.95339	0
45.	4GH9-zinc_1529208-0.pdb	-53.2157	-50.6551	-2.56059	0
46.	4GH9-zinc_3978625-1.pdb	-52.6161	-44.9077	-7.70844	0
47.	4GH9-zinc_1529210-0.pdb	-52.3723	-44.0682	-8.30415	0
48.	4GH9-zinc_57736-0.pdb	-50.9547	-42.4932	-8.46152	0
49.	4GH9-zinc_967513-0.pdb	-45.2401	-45.2401	0	0
50.	4GH9-zinc_1530846-0.pdb	-41.9469	-39.0265	-2.92037	0

Table 6: Results of docking between different ligands and targeted protein in the form of total binding energy for Ebola

SN	Compound	Energy	VDW	HBond	Elec
1.	**2I8B_zinc_14587259-0.pdb**	**-98.7443**	**-80.971**	**-17.7733**	**0**
2.	2I8B_zinc_3954302-1.pdb	-94.9113	-77.2478	-17.6635	0
3.	2I8B_zinc_3869685-1.pdb	-94.3705	-68.4648	-25.9057	0
4.	2I8B_zinc_1604019-0.pdb	-93.8283	-89.5826	-4.24574	0
5.	2I8B_zinc_3777403-1.pdb	-93.7607	-76.6086	-17.1521	0
6.	2I8B_zinc_6845904-1.pdb	-92.5827	-92.5827	0	0
7.	2I8B_zinc_3779067-0.pdb	-91.6882	-87.4968	-4.19138	0
8.	2I8B_zinc_897714-0.pdb	-88.1091	-78.931	-9.17809	0
9.	2I8B_zinc_608233-1.pdb	-86.614	-85.7869	-0.827105	0
10.	2I8B_zinc_3830891-0.pdb	-85.8901	-54.1061	-31.784	0
11.	2I8B_zinc_3881796-0.pdb	-85.4147	-72.9094	-12.5053	0
12.	2I8B_zinc_3978650-1.pdb	-84.2864	-78.1801	-6.1063	0
13.	2I8B_zinc_6393492-1.pdb	-82.8393	-80.3393	-2.5	0
14.	2I8B_zinc_1530575-1.pdb	-81.94	-77.2103	-4.72967	0
15.	2I8B_zinc_6920384-1.pdb	-81.4375	-75.4375	-6	0
16.	2I8B_zinc_4081455-0.pdb	-81.231	-77.4227	-3.80834	0
17.	2I8B_zinc_3978429-1.pdb	-80.715	-78.215	-2.5	0
18.	2I8B_zinc_3872446-0.pdb	-80.5565	-48.9194	-31.6371	0
19.	2I8B_zinc_3861087-1.pdb	-80.4972	-70.9972	-9.5	0
20.	2I8B_zinc_6845860-1.pdb	-80.0832	-73.8497	-5.10982	-1.12368
21.	2I8B_zinc_899213-0.pdb	-79.7457	-74.1854	-5.56033	0
22.	2I8B_zinc_4095717-0.pdb	-79.7157	-77.2157	-2.5	0
23.	2I8B_zinc_4501378-0.pdb	-78.7224	-71.8269	-6.89551	0
24.	2I8B_zinc_3978827-0.pdb	-77.9771	-72.858	-5.11911	0
25.	2I8B_zinc_4474564-1.pdb	-74.7347	-64.3737	-10.361	0
26.	2I8B_zinc_13585362-0.pdb	-74.257	-59.0965	-15.1605	0
27.	2I8B_zinc_3872206-0.pdb	-73.6113	-57.4537	-16.1576	0
28.	2I8B_zinc_3875425-0.pdb	-73.5029	-62.2982	-11.2047	0
29.	2I8B_zinc_3978625-0.pdb	-73.0231	-64.6009	-8.42221	0
30.	2I8B_zinc_57908-0.pdb	-72.5458	-52.1334	-20.4124	0
31.	2I8B_zinc_6361655-0.pdb	-70.1151	-56.261	-13.8541	0
32.	2I8B_zinc_6072466-0.pdb	-69.4545	-58.5862	-10.8683	0
33.	2I8B_zinc_5842977-1.pdb	-69.3816	-61.9331	-7.44849	0
34.	2I8B_zinc_35525-1.pdb	-69.3438	-64.8157	-4.52806	0
35.	2I8B_zinc_1670024-0.pdb	-69.2799	-69.2799	0	0
36.	2I8B_zinc_3847491-0.pdb	-68.2784	-63.8823	-4.3961	0
37.	2I8B_zinc_1084-0.pdb	-67.991	-60.991	-7	0
38.	2I8B_zinc_1504-0.pdb	-67.4362	-52.8195	-14.6167	0
39.	2I8B_zinc_158743-0.pdb	-66.7454	-51.4738	-15.2716	0
40.	2I8B_zinc_57731-0.pdb	-65.5887	-64.8496	-0.739117	0
41.	2I8B_zinc_1411-0.pdb	-65.2578	-56.7578	-8.5	0
42.	2I8B_zinc_74709-1.pdb	-64.303	-50.982	-13.321	0
43.	2I8B_zinc_1529210-0.pdb	-63.3082	-51.9475	-11.3607	0
44.	2I8B_zinc_1529208-1.pdb	-62.0281	-53.6404	-8.38774	0
45.	2I8B_zinc_5766182-1.pdb	-60.5984	-48.5984	-12	0
46.	2I8B_zinc_14806511-0.pdb	-57.1063	-49.3211	-7.78519	0
47.	2I8B_zinc_57736-0.pdb	-57.0708	-53.5708	-3.5	0
48.	2I8B_zinc_2557133-1.pdb	-52.3277	-46.4999	-5.82785	0
49.	2I8B_zinc_1530846-0.pdb	-49.948	-47.5826	-2.36536	0
50.	2I8B_zinc_967513-1.pdb	-48.1654	-48.1654	0	0

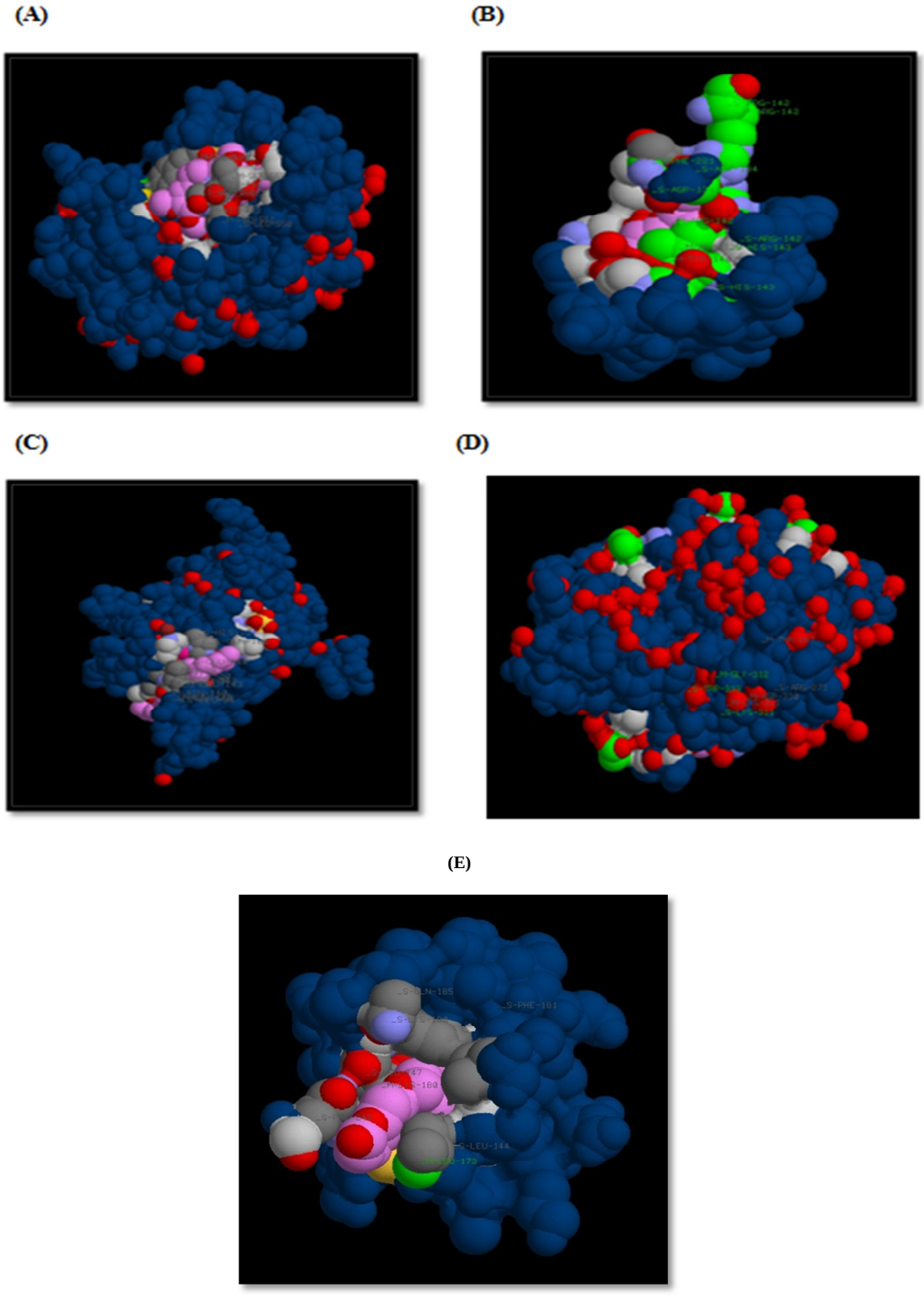


Figure 3: Docking results of (A) Junin virus (B) Hanta virus (C) Dengue virus (D) Marburg virus and (E) Ebola virus with phytochemicals marmin, delphinidin chloride, squalene and palmatine shown similar results for Marburg and Ebola respectively

CONCLUSION

Now a day's molecular docking play a key role in understanding drug receptor interaction, which further help in designing novel, or potent inhibitors through drug receptor interaction mechanism. Till date, no authentic antiviral drug or vaccine is available these viruses except Candid1 against junin, with some side effects. In the present study, we persuaded out docking studies on the 50 bioactive compounds to different proteins or targets for 5 severe viruses, with the aim to propose such components which possesses the property to inhibit the activity of mentioned life-threatening viruses. Bioactive components such as marmin, delphinidin chloride, squalene, palmatine shows maximum binding energy whereas d-limonene and allicin showed minimum binding energy for selected viruses.

Acknowledgement
We would like to thank the Graphic Era University, Dehradun, Uttarakhand, India for supporting this research.

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