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Design and Identification of Lead Compounds Targeting Nipah G Attachment Glycoprotein by *In Silico* Approaches

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Authors' contributions

This work was carried out in collaboration among all authors. 'All authors read and approved the final manuscript.

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ABSTRACT

Nipah virus (NiV) caused several outbreaks in Asian countries, including the latest one from the Kerala state of India. There is no drug available against NiV till now, despite its urgent requirement. There are reports about the anti-influenza viral drug Favipiravir, which has positively affected the Nipah virus *in vitro* models. In the current work, we have provided a computational screening for NiV inhibitors. Twenty-two designed compounds from favipiravir and Nipah glycoprotein, 3D11, were chosen and performed molecular docking to analyse the various conformations and interactions with the amino acids; further, their physicochemical and ADMET properties were also computed. The compound 5_Favipiravir have an excellent docking score (-6.16 kcal/mol), followed by compound 4_Favipiravir and 19_Favipiravir with docking score of -5.50 and -5.38 kcal/mol respectively. The three compounds had the respective heterocyclic moieties such as pyrazole, imidazole and pyrazinone. All the twenty-two designed compounds obey the Lipinski rule of five, which infer that they will not have problems with oral bioavailability. Thus, it is concluded that the incorporated heterocyclic groups in favipiravir can add to the anti-Nipah activity; hence it can act as future leads for the treatment for the disease caused by Nipah virus.

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Keywords: Nipah virus; Favipiravir; Molecular docking; Physicochemical & ADMET properties.

1. INTRODUCTION

Nipah virus (NiV) is an evolving virus that can cause severe respiratory disease and deadly encephalitis in humans, including paramyxovirus (Henipavirus, Paramyxovirinae subfamily, family Paramyxoviridae, the order of Mononegavirales). Several significant individual outbreaks occurred in the twenty-first century beginning in Bangladesh and India in 2001 [1]. Similar explosions were also reported in two villages in the Philippines in 2014. In Kerala, a southern Indian state, the latest uprising started in May 2018 [2,3].

Therapy is limited to treatment and support. In preventing hospital-acquired infections, standard infection prevention procedures and barrier nursing strategies are critical as NiV encephalitis can be transmitted from person to person. Ribavirin, a hepatitis C antiviral drug, has also proved helpful *in vitro*, but to date, human trials have not been completed with doubt regarding the clinical usefulness of ribavirin [4,5]. Ribavirin is a therapy that is approved or tolerated for a variety of viral infections [6]. In vitro experiments showed that ribavirin acts against replication of Hendra and Nipah viruses [7,8].

Furthermore, it was earlier demonstrated that anti-malarial drug chloroquine blocks the essential proteolytic processing required to develop the structure and function of Hendra F glycoprotein virus and chloroquine [9] and, not surprisingly, was later shown to inhibit Nipah and Hendra infection in cell culture [10]. There have been two experiments in hamsters and one in non-human primates (African Green Monkey (A Green monkey)) that only delayed treatment with ribavirin but not prevented death following infection by Nipah Virus [11,12]. The use in the post-exposure therapy in ferret models of a human monoclonal antibody targeting Nipah G glycoprotein has been tested and has proved to be effective [13,14].

The chemical modification of the pyrazine analogue initially screened for *in vitro* anti-influenza virus activity in cells discovered Favipiravir [15]. Favipiravir inhibits influenza viral RNA polymerase [16] and is a versatile and effective inhibitor that works against all subtypes and strains of the flu virus, including those susceptible or immune to neuraminidase and M2 inhibitors on the market. Antiviral activities against other RNA viruses were also demonstrated by Favipiravir [17]. These data indicate that favipiravir is potent medicine for treating influenza virus infections and various RNA viruses.

Favipiravir disrupted the viral genome in the centre of the replication process in a drug additive test. Antiviral favipiravir action was attenuated by purine nucleosides or purine bases, suggesting that favipiravir interacts with purine nucleosides instead of pyrimidine nucleosides [16].

Nowadays, computer‑aided drug design is one of the essential techniques of rational drug design. The *in silico* study involves different computational methods which help to reduce the time and cost of the drug discovery process [18]. The high-throughput automated screening method is time-consuming, as more compounds must be trialled. Structure‑based drug design is helpful to find out the new lead compound, which is active against the target. This process required a lesser number of compounds that may take into the trial [19].

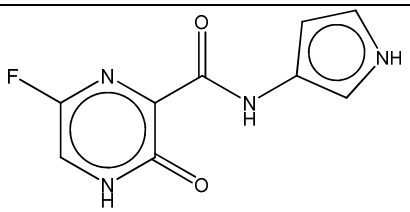
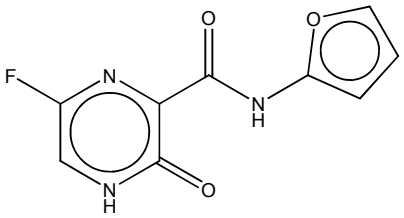
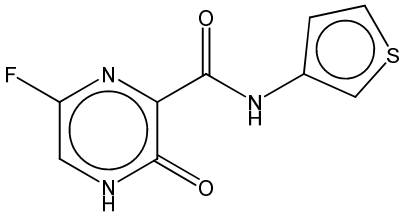
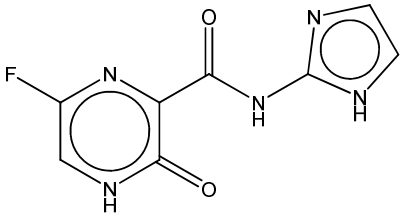
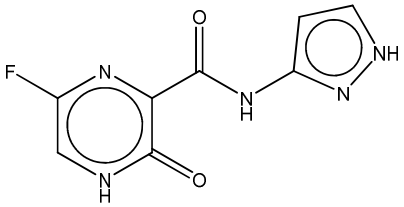
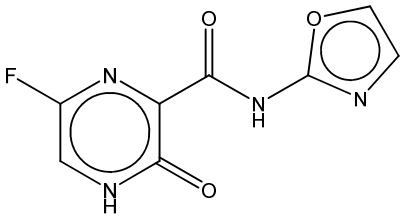
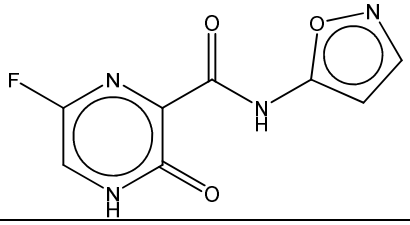
In continuation of the *in silico* studies conducted earlier [20,21], in this study, we have designed 22 compounds of favipiravir containing pyrazine as the moiety and other heterocyclic rings to identify novel inhibitors of NiV using different *in silico* methods. Molecular docking, physicochemical properties and ADMET properties were determined by using Schrodinger software. The comparison of *in silico* results was made with standard drug favipiravir.

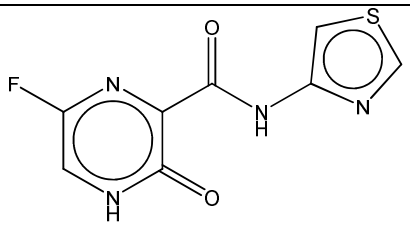
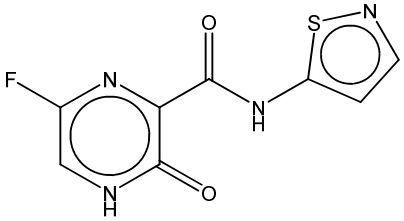
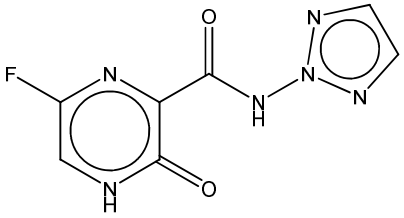
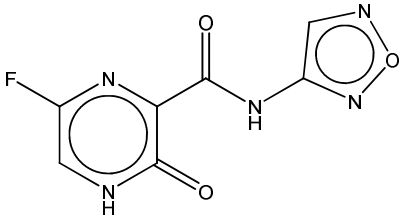
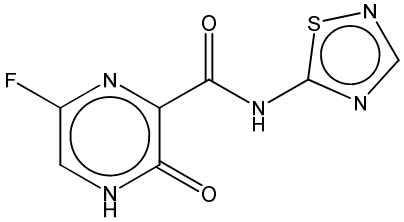
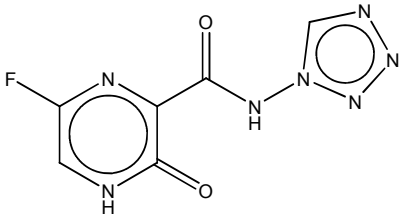
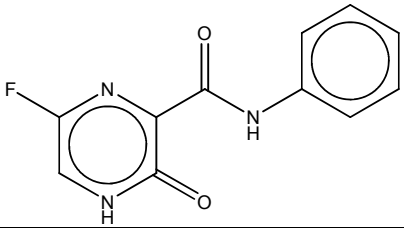
2. METHODOLOGY

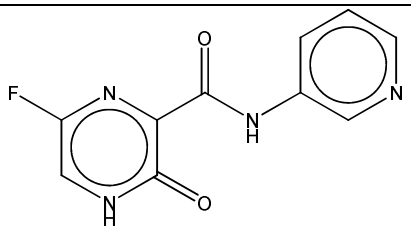
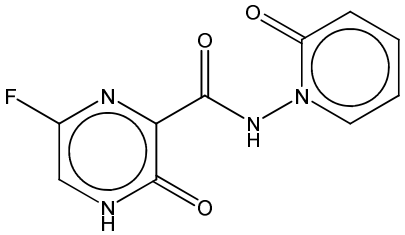
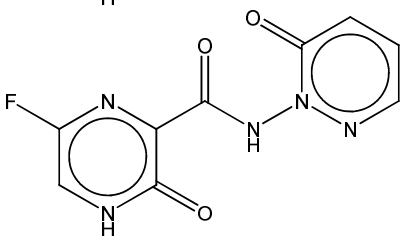
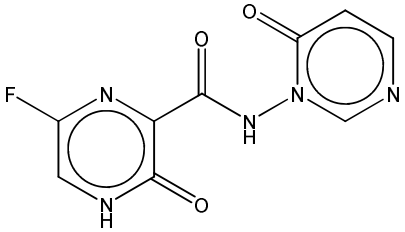
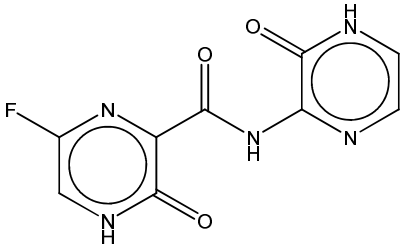
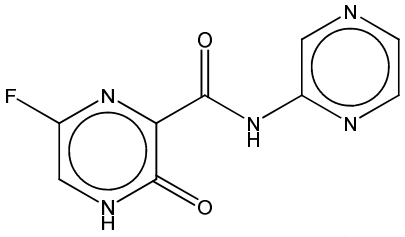
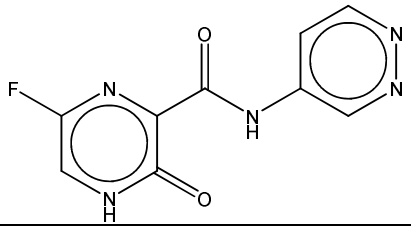
2.1 Reaction Enumeration

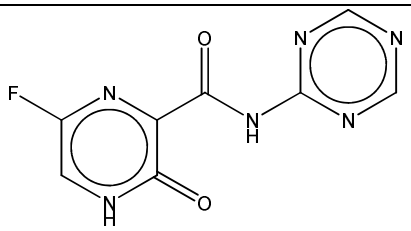
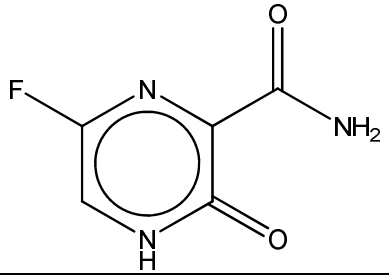
In this method, numerous compounds can be generated as a derivative of the parent compound. There is a possibility to replace the substituent based on the chemical nature of the compounds. In this study, the hydrogen atom in the amino group of Favipiravir was replaced with aromatic monocyclic groups available in Schrodinger enumeration databases [22] (Table 1).

Table 1. Chemical structures and SMILES of the designed compounds

S. NO.	Ligand ID	Chemical structure	R1
1.	1_ Favipiravir		pyrrole
2.	2_Favipiravir		furan
3.	3_Favipiravir		thiophene
4.	4_Favipiravir		imidazole
5.	5_Favipiravir		pyrazole
6.	6_Favipiravir		oxazole_2
7.	7_Favipiravir		isoxazole_2

S. NO.	Ligand ID	Chemical structure	R1
8.	8_Favipiravir		thiazole_2
9.	9_Favipiravir		isothiazole_2
10.	10_Favipiravir		125_triazole
11.	11_Favipiravir		125_oxadiazole
12.	12_Favipiravir		124_thiadiazole
13.	13_Favipiravir		tetrazole
14.	14_Favipiravir		benzene

S. NO.	Ligand ID	Chemical structure	R1
15.	15_Favipiravir		pyridine
16.	16_Favipiravir		pyridone
17.	17_Favipiravir		pyridazinone
18.	18_Favipiravir		pyrimidone-1
19.	19_Favipiravir		pyrazinone
20.	20_Favipiravir		pyrazine
21.	21_Favipiravir		pyridazine

S. NO.	Ligand ID	Chemical structure	R1
22.	22_Favipiravir		135_triazine
23.	Favipiravir		pyrazine

2.2 Ligand Preparation

All the ligands were neutralised, desalted, prevented from tautomers generation to retain a specific chirality by the Ligprep application tool in Schrodinger [23]. Only one structure was generated per ligand.

2.3 Protein Preparation

The specific Nipah protein 3D11 was imported from the protein data bank (PDB) [24] and processed by the Protein Preparation Wizard application tool in Schrodinger. Pre-processing of the protein was done by assigning bond orders by adding hydrogen, creating zero-order bonds to metals, creating disulphide bonds, filling the missing side chain and loops by using the prime module. All the water molecules were deleted beyond 5 Å, from the hetero groups. The hetero states of the ligand were maintained in the pH range 7±2.

2.4 Receptor Grid Generation

Grid generation specifies the 3D (X,Y,Z-axis) location where the ligand binds. A grid was generated for the minimised protein by using the tool Receptor Grid Generation in Schrodinger.

2.5 Ligand Docking

Ligand docking was performed by Glide-XP application in Schrodinger [25]. In the Glide –XP panel, the receptor grid generated was uploaded, and the prepared ligands were imported as out.maegz file to the working panel. In the precision tab, XP (extra precision) was selected, and the method adopted was flexible docking in ligand sampling [24].

2.6 Physicochemical Properties

The physicochemical properties were calculated by QikProp application of Schrodinger software [26]. The prepared ligands were selected and incorporated into the Qikprop tool and processed. The properties Molecular weight, Log P, QPlogPo/w, donor-HB, accept-HB, which analyse Lipinski Rule of five [27] were assessed.

2.7 ADMET Properties

The ADMET properties were computed by the QikProp application of Schrodinger software [28]. The prepared ligand was selected and incorporated into the Qikprop tool and processed. The features such as QPPCaco, % Human oral absorption, QPlogKhsa, SASA, QPlogHERG was analysed.

3. RESULTS AND DISCUSSION

3.1 Molecular Docking

In the present study, twenty-two designed compounds and Nipah glycoprotein, 3D11, were chosen and performed molecular docking to analyse the various conformations and interactions with the amino acids (Fig. 1). On further analysis of the results, thirteen favipiravir derivatives (5_Favipiravir, 4_Favipiravir, 19_Favipiravir, 8_Favipiravir, 15_Favipiravir, 12_Favipiravir, 18_Favipiravir, 20_Favipiravir,

22_Favipiravir, 1_Favipiravir, 3_Favipiravir, 6_Favipiravir, 21_Favipiravir) were found to have docking scores higher than the standard favipiravir, suggesting that they might have an excellent binding with the Nipah virus protein. The docking scores and amino acid interactions are tabulated in Tables 2 & 3; 2D and 3D conformations are reported in Figs. 2-4.

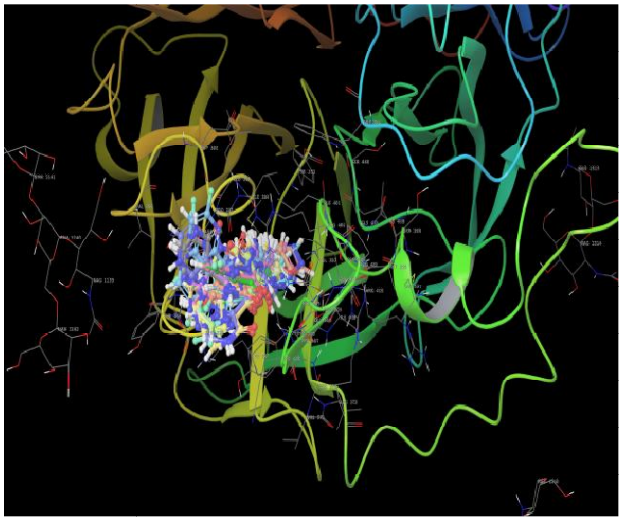


Fig. 1. 3D Conformations of twenty-two designed ligands within the pockets of 3D11 protein

Table 2. Docking results of ligand interacting with the active site of 3D11

S.No	Ligand ID	Glide XP docking score (kcal/mol)	Glide energy	Heterocyclic group
1.	5_Favipiravir	-6.16	-32.86	Pyrazole
2.	4_Favipiravir	-5.50	-36.06	Imidazole
3.	19_Favipiravir	-5.38	-37.21	Pyrazinone
4.	8_Favipiravir	-4.37	-31.05	Thiazole_2
5.	15_Favipiravir	-4.37	-32.19	Pyridine
6.	12_Favipiravir	-4.35	-31.74	124_thiadiazole
7.	18_Favipiravir	-4.31	-31.55	pyrimidone-1
8.	20_Favipiravir	-4.31	-31.58	Pyrazine
9.	22_Favipiravir	-4.12	-31.43	135_triazine
10.	1_ Favipiravir	-3.92	-30.85	Pyrrole
11.	3_Favipiravir	-3.85	-32.14	Thiophene
12.	6_Favipiravir	-3.75	-32.03	oxazole_2
13.	21_Favipiravir	-3.73	-31.76	Pyridazine
14.	7_Favipiravir	-3.44	-33.99	isoxazole_2
15.	2_Favipiravir	-3.41	-32.28	Furan
16.	10_Favipiravir	-3.41	-32.49	125_triazole
17.	13_Favipiravir	-3.29	-37.39	Tetrazole
18.	11_Favipiravir	-3.28	-32.21	125_oxadiazole
19.	9_Favipiravir	-3.24	-31.72	isothiazole_2
20.	17_Favipiravir	-3.09	-33.25	Pyridazinone
21.	16_Favipiravir	-2.98	-30.63	Pyridone
22.	14_Favipiravir	-1.81	-27.61	Benzene
23.	Favipiravir	-3.70	-19.23	Standard

Table 3. Ligand interactions with the protein 3D11

S.No	Ligand ID	Hydrophobic interaction with ligand	Polar interaction with ligand	H-bond	pi-cation
1.	5_Favipiravir	Tyr 309, Ile 304, Ile 401, Phe 369, Tyr 401, Ile 408, Leu 409	Thr 308, Ser 307, Ash 306, Ser 405, Hid 406	Thr 308, Hid 406, Tyr 407	-
2.	4_Favipiravir	Tyr 308, Leu 305, Ile 304, Leu 409, Phe 369, Ile 408 Tyr 407, Ile 401	Thr 308, Ser 307, Asn 306, Hid 406, Ser 405	Thr 308, Ile 304, Hid 406, Arg 402	-
3.	19_Favipiravir	Tyr 309, Leu 305, Ile 304, Phe 369, Ile 401, Tyr 407, Leu 409	Thr 308, Ser 307, Asn 306, Ser 405, Hid 406	Ser 307, Hid 406	Arg 402
4.	8_Favipiravir	Tyr 309, Leu 305, Ile 304, Ile 401, Phe 369, Tyr 407, Leu 409	Thr 308, Ser 307, Asn 306, Ser 405, Hid 406	Ile 304, Hid 406	Arg 402
5.	15_Favipiravir	Tyr 309, Leu 305, Ile 304, Leu 409 Tyr 407, Ile 401	Thr 308, Ser 307, Asn 306, Hid 406, Ser 405	Thr 308, Tyr 407	Arg 402
6.	12_Favipiravir	Tyr 309, Leu 305, Ile 304, Ile 401, Phe 369, Tyr 307, Leu 409	Thr 308, Ser 307, Asn 306, Ser 405, Hid 406	Ile 304, Hid 406	Arg 402
7.	18_Favipiravir	Tyr 309, Leu 305, Ile 304, Tyr 407, Ile 401	Thr 308, Ser 307, Asn 306, Hid 406, Ser 405	Ser 407, Asn 406, Tyr 407, Arg 402	Arg 402
8.	20_Favipiravir	Tyr 309, Leu 305, Ile 304, Tyr 407, Ile 401	Thr 308, Ser 307, Asn 306, Hid 406, Ser 405	Thr 308, Tyr 407	Arg 402
9.	22_Favipiravir	Tyr 309, Leu 305, Ile 304, Ile 401, Tyr 407, Leu 409	Thr 308, Ser 307, Asn 306, Hid 406, Ser 405	Hid 406, Ile 304	Arg 402
10.	1_ Favipiravir	Tyr 309, Leu 305, Ile 304, Tyr 407, Ile 401	Thr 308, Ser 307, Asn 306, Hid 406, Ser 405, Asn 404	Hid 406, Arg 402, Ile 304	Arg 402
11.	3_Favipiravir	Tyr 309, Leu 305, Ile 304, Tyr 407, Ile 401, Leu 409, Phe 369	Thr 308, Ser 307, Asn 306, Hid 406, Ser 405	Hid 406	Arg 402
12.	6_Favipiravir	Tyr 309, Leu 305, Ile 304, Tyr 407, Ile 401, Leu 409, Phe 369	Thr 308, Ser 307, Asn 306, Hid 406, Ser 405	Hid 406, Ile 304, Thr 308	Arg 402
13.	21_Favipiravir	Tyr 309, Leu 305, Ile 304, Tyr 407, Ile 401, Leu 409, Phe 369	Thr 308, Ser 307, Asn 306, Hid 406, Ser 405	Hid 406, Ile 304	Arg 402
14.	7_Favipiravir	Tyr 309, Ile 304, Tyr 407, Ile 401, Ile 408, Leu 409, Phe 369	Thr 308, Ser 307, Asn 306, Hid 406, Ser 405	Hid 406, Ile 401, Tyr 407	Arg 402
15.	2_Favipiravir	Tyr 309, Ile 304, Tyr 407, Ile 401, Ile 408, Leu 409, Phe 369	Thr 308, Ser 307, Asn 306, Hid 406, Ser 405	Hid 406, Tyr 407	Arg 402
16.	10_Favipiravir	Tyr 309, Leu 305, Ile 304, Tyr 407, Ile 401, Leu 409, Phe 369	Thr 308, Ser 307, Asn 306, Hid 406, Ser 405	Hid 406, Thr 308, Ile 304	Arg 402
17.	13_Favipira	Tyr 309, Ile 304, Tyr 407,	Thr 308, Ser 307,	Hid 406, Tyr	Arg

S.No	Ligand ID	Hydrophobic interaction with ligand	Polar interaction with ligand	H-bond	pi-cation
	vir	Ile 401, Leu 409, Phe 369	Asn 306, Hid 406, Ser 405	407, Ile 401	402
18.	11_Favipiravir	Tyr 309, Leu 305, Ile 304, Tyr 407, Ile 408, Ile 401, Leu 409, Phe 369	Thr 308, Ser 307, Asn 306, Hid 406, Ser 405	Leu 305, Hid 406, Tyr 407	Arg 402
19.	9_Favipiravir	Ile 304, Leu 305, Tyr 309, Ile 401, Tyr 407, Leu 409	Thr 308, Ser 307, Asn 306, Hid 406, Ser 405	Tyr 407	Arg 402
20.	17_Favipiravir	Tyr 309, Leu 305, Ile 304 Ile 401, Tyr 407, Leu 409	Thr 308, Ser 307, Asn 306, Ser 405, Hid 406,	Thr 308, Hid 406	Arg 402
21.	16_Favipiravir	Tyr 309, Leu 305, Ile :304, Tyr :407, Ile :401	Thr 308, Ser 307, Asn 306, Hid 406, Ser 405, Asn 404	Tyr 407, Hid 406, Arg 402	Arg 402
22.	14_Favipiravir	Tyr 309, Leu 305, Ile 304, Tyr 407, Ile 401	Thr 308, Ser 307, Asn 306, Hid 406, Ser 405	Thr 308	Arg 402
23.	Favipiravir	Tyr 309, Ile 304, Leu 409, Tyr 407, Ile 401	Thr 308, Ser 307, Asn 306, Hid 406, Ser 405	Ser 307, Tyr 407, Hid 406	Arg 402

3.2 Binding of 5_Favipiravir with 3D11

The active amino acids in the protein 3D11, which made hydrophobic interaction with the 5_Favipiravir was found to be Tyr 309, Ile 304, Ile 401, Phe 369, Tyr 401, Ile 408, Leu 409, polar interaction was Thr 308, Ser 307, Asp 306, Ser 405, Hid 406 and hydrogen bond was Thr 308, Hid 406, Tyr 407. It showed a docking score of -6.165 kcal/mol compared with the standard drug Favipiravir (-3.706 kcal/mol) (Figs. 2a & 2b).

3.3 Binding of 4_Favipiravir with 3D11

The docking score of 4_Favipiravir with 3D11 is -5.501 kcal/mol compared with the standard drug Favipiravir (-3.706 kcal/mol). The amino acids in the protein 3D11 which are responsible for hydrophobic interactions are Tyr 308, Leu 305, Ile 304, Leu 409, Phe 369, Ile 408, Tyr 407, Ile 401; polar interactions are Thr 308, Ser 307, Asn 306, Hid 406, Ser 405; and hydrogen bondings are Thr 308, Ile 304, Hid 406, Arg 402 (Figs. 3a & 3b).

3.4 Binding of 19_Favipiravir with 3D11

The compound 19_Favipiravir interacted with the protein 3D11 with the docking score of -5.38 kcal/mol. The respective active amino acids Tyr 309, Leu 305, Ile 304, Phe 369, Ile 401, Tyr 407, Leu 409 made hydrophobic interaction with ligand; Thr 308, Ser 307, Asn 306, Ser 405, Hid 406 are responsible for polar interaction with ligand; Ser 307, Hid 406 for H-bond; and the particular amino acid for Arg 402 pi-cation (Figs. 4a & 4b).

3.5 Physicochemical Properties and Rule of Five Properties

All the compounds have their molecular weight below 500 ranging from 150-260. The calculated log P value of the compounds is below 5. The compounds under investigation possess hydrogen bond donors (<5) and hydrogen bond acceptors (<10) within the limit. Based on the experimental values (Table 4), it was found that all the compounds have values within the normal range, and there is no violation of Lipinski's rule of five. Hence the compounds are expected to possess excellent oral bioavailability.

3.6 *In silico* ADMET Studies

The results show that compounds have better scores for Caco-2 permeability, human oral absorption, Total solvent accessible surface area, human serum albumin binding (Table 5).

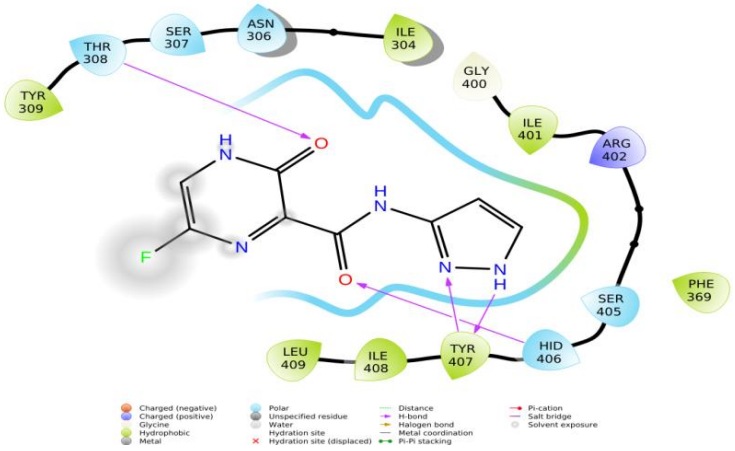


Fig. 2a. 2D Conformation of 5_Favipiravir with 3D11 protein

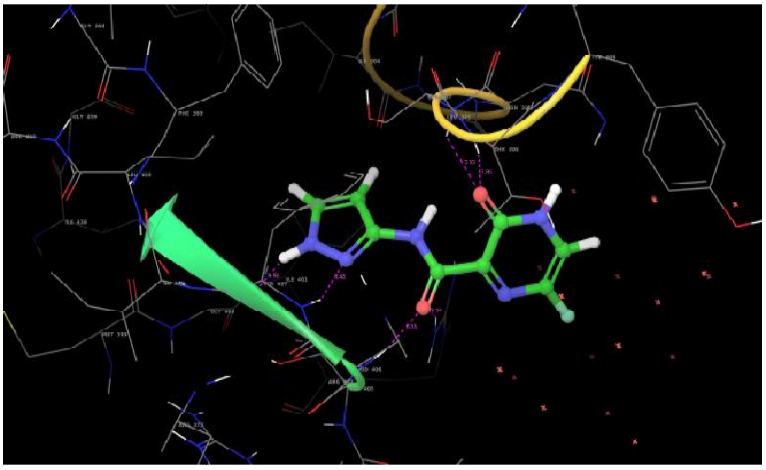


Fig. 2b. 3D Conformation of 5_Favipiravir with 3D11 protein

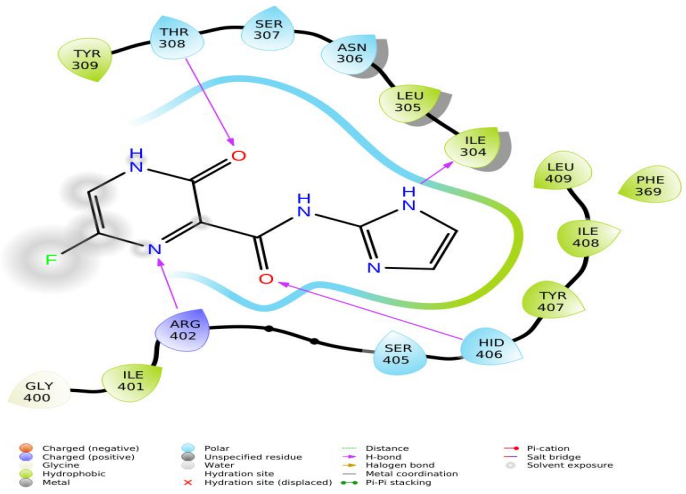


Fig. 3a. 2D Conformation of 4_Favipiravir with 3D11 protein

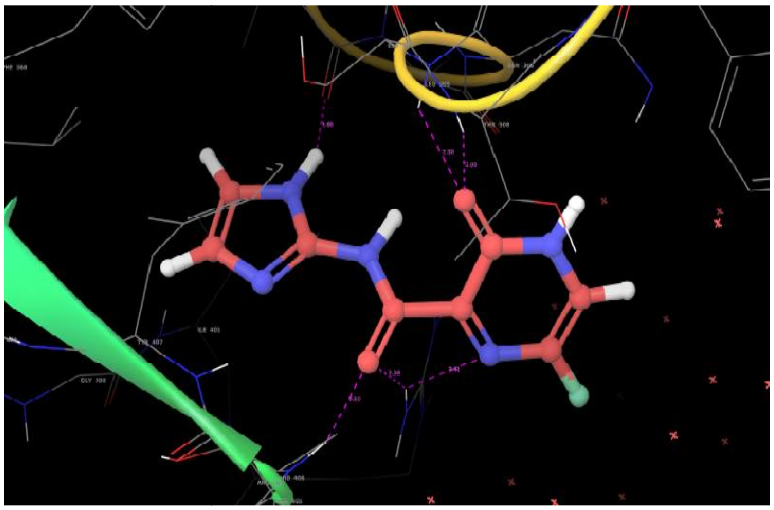


Fig. 3b: 3D Conformation of 4_Favipiravir with 3D11 protein

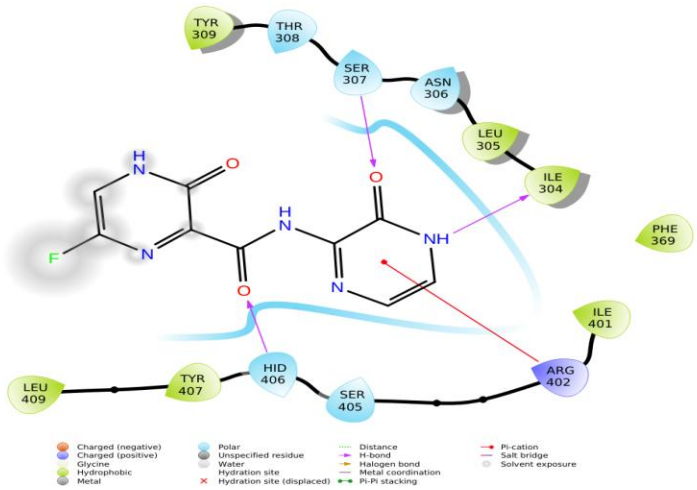


Fig. 4a. 2D Conformation of 19_Favipiravir with 3D11 protein

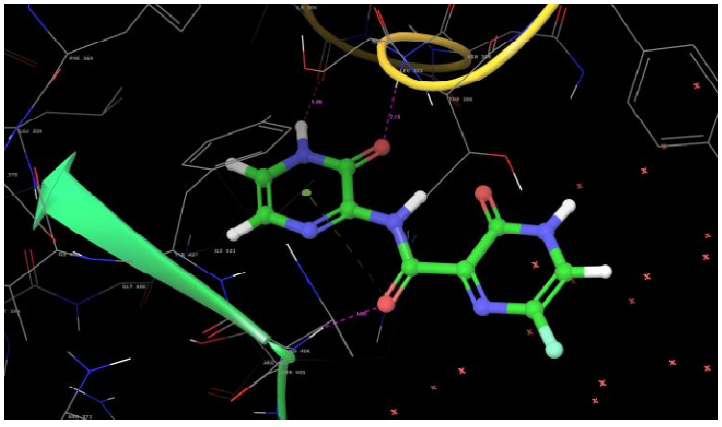


Fig. 4b. 3D Conformation of 19_Favipiravir with 3D11 protein

Table 4. Physicochemical properties of designed compounds

S.No	Ligand ID	Molecular weight	Log P QPlogPo/w	Donor HB	acceptHB	PSA	Volume	rotor
1.	1_ Favipiravir	222.17	1.09	1	4.5	101.67	679.24	2
2.	2_Favipiravir	223.16	0.96	0	4.5	96.55	652.07	2
3.	3_Favipiravir	239.22	1.89	0	4	87.45	701.9	2
4.	4_Favipiravir	223.16	0.93	0	4.5	115.54	668.16	2
5.	5_Favipiravir	223.16	0.25	1	5.5	117.88	667.93	2
6.	6_Favipiravir	224.15	-0.17	0	6	110.71	643.75	2
7.	7_Favipiravir	224.15	-0.14	0	5.5	115.39	658.81	2
8.	8_Favipiravir	240.21	0.64	0	5.5	100.31	692.72	2
9.	9_Favipiravir	240.21	0.94	0	5.5	102.80	690.09	2
10.	10_Favipiravir	224.15	-1.28	0	8	123.08	662.64	2
11.	11_Favipiravir	225.13	-0.98	0	6.5	134.14	645.72	2
12.	12_Favipiravir	241.19	-0.22	0	6.5	115.89	681.29	2
13.	13_Favipiravir	225.14	-2.24	0	9	141.58	650.65	2
14.	14_Favipiravir	233.20	2.01	0	4	87.18	734.08	2
15.	15_Favipiravir	234.18	0.63	0	5.5	100.13	719.83	2
16.	16_Favipiravir	250.18	0.15	0	6.5	119.78	746.36	2
17.	17_Favipiravir	251.17	-0.10	0	6.5	134.32	736.88	2
18.	18_Favipiravir	251.17	-0.88	0	8	132.63	733.63	2
19.	19_Favipiravir	251.17	-0.40	1	7.5	140.89	729.52	2
20.	20_Favipiravir	235.17	-0.06	0	6.5	112.10	710.12	2
21.	21_Favipiravir	235.17	-0.48	0	7	116.08	706.66	2
22.	22_Favipiravir	236.16	-0.90	0	7.5	125.05	697.30	2
23.	Favipiravir	157.10	-0.40	1	4	104.95	479.10	1

Table 5. Predicted *in silico* ADMET properties of designed compounds

S.No:	Ligand ID	QPPCaco	% Human oral absorption	QPlogKhsa	SASA	Rule of five	Rule of three
1.	1_ Favipiravir	241.05	76.01	-0.42	427.51	0	0
2.	2_ Favipiravir	442.62	79.96	-0.77	405.89	0	0
3.	3_ Favipiravir	488.16	86.16	-0.49	438.51	0	0
4.	4_ Favipiravir	148.07	71.28	-0.73	422.93	0	0
5.	5_ Favipiravir	124.55	65.93	-0.61	422.39	0	0
6.	6_ Favipiravir	263.69	69.28	-1.20	402.63	0	0
7.	7_ Favipiravir	106.36	62.36	-1.02	418.44	0	0
8.	8_ Favipiravir	311.78	75.34	-0.92	435.19	0	0
9.	9_ Favipiravir	208.38	73.97	-0.80	435.75	0	0
10.	10_ Favipiravir	123.58	56.88	-1.68	420.02	0	0
11.	11_ Favipiravir	54.08	52.22	-1.33	409.07	0	0
12.	12_ Favipiravir	133.8	63.68	-1.22	433.66	0	0
13.	13_ Favipiravir	43.03	43.04	-1.98	414.66	0	0
14.	14_ Favipiravir	499.11	87.03	-0.40	455.04	0	0
15.	15_ Favipiravir	270.53	74.17	-0.84	447.20	0	0
16.	16_ Favipiravir	168.00	67.69	-1.03	460.59	0	0
17.	17_ Favipiravir	99.13	62.05	-1.06	456.99	0	0
18.	18_ Favipiravir	91.90	56.88	-1.47	453.78	0	0
19.	19_ Favipiravir	58.34	56.17	-0.82	453.00	0	0
20.	20_ Favipiravir	183.49	67.06	-1.14	443.57	0	0
21.	21_ Favipiravir	122.98	61.50	-1.28	440.37	0	0
22.	22_ Favipiravir	90.32	56.65	-1.44	439.99	0	0
23.	Favipiravir	111.54	61.2	-0.74	318.63	0	0

4. CONCLUSIONS

Twenty-two compounds were designed from the compound favipiravir and screened for their anti-Nipah activity by molecular docking and their ADMET properties were computed. The compound 5_Favipiravir have an excellent docking score, i.e., -6.16 kcal/mol, followed by compound 4_Favipiravir and 19_Favipiravir with docking score of -5.50 and -5.38 kcal/mol respectively. The three compounds had the respective heterocyclic moieties such as pyrazole, imidazole and pyrazinone. On further analysis of the results, thirteen favipiravir derivatives were found to have docking scores higher than the standard favipiravir, suggesting that they might have an excellent binding with the Nipah virus protein. All the twenty-two designed compounds obey the Lipinski rule of five, which infer that they will not have problems with oral bioavailability. Thus, it is concluded that the incorporated heterocyclic compounds can add to the anti-Nipah activity; hence it can act as future leads for the treatment for the disease caused by the Nipah virus.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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