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Research Article

Molecular Docking studies on possible Neuraminidase Inhibitors of Influenza Virus

Abstract

Background: Influenza generally known as flu is due to viruses that contaminate the respiratory region. It can result in light to cruel sickness, and may cause death. The influenza pandemic of 1918-1919 took life of a lot more people than the World War 1. Peramivir that inhibits the purpose of the viral neuraminidase protein of influenza virus, therefore stopping the virus from replicating through budding from the host cell has been shown to have hindrance against virus. The neuraminidase enzyme is a glycoside hydrolyses enzyme that is shown on the exterior. It allows the virus to be free from the host cell and slice sialic acid groups from glycoproteins and is necessary for influenza virus reproduction.

Methods: This study concentrates on the in silico virtual screening and molecular docking examination for probable neuraminidase blockers by peramivir like compounds recovered by the ZINC database. ADME-Toxicity examination is done by in silico methods.

Results: Molecular docking outcomes propose that modified ligand Anamivire have improved binding attraction than peramivir and its derivatives i.e. ZINC3981610, ZINC 40709762.

Conclusion: Modified ligand Anamivire is shown to have resistance against neuraminidase enzyme and bioavailability troubles than ZINC3981610, ZINC40709762 and peramivir.

Introduction

The flu is the infectious respiratory sickness caused by influenza viruses [1]. Flu viruses are separated into 3 kinds chosen A, B and C [2]. Influenza types A and B are cause for outbreaks of respiratory sickness and frequently result in death. Type C generally result in very light respiratory illness it does not result in outbreaks and does not have the cruel public health impact. Influenza viruses are members of the family Orthomyxoviridae and include a genome of negative-strand RNA units [3]. The influenza virus is based on the sixteen hemagglutinin (HA) and nine neuraminidase (NA) encircle protein [4]. HA protein act a fundamental part in the addition of the virus to host cell membrane surface glycoprotein or glycolipid by multivalent connections to the sialoglycans [5], and making possible the spread of newly synthesized. Virus in the host and is an important target for controlling disease succession. The signs of disease vary from fever and anorexia to coughing, rhinorrhea, gastrointestinal trouble.

The neuraminidase enzymes are glycoside hydrolase enzymes (EC 3.2.1.18) present on the exterior of influenza viruses facilitate the virus to be set free from the host cell and slice sialic acid groups from glycoproteins and are essential for influenza virus reproduction. It also acts a vital part in making possible the distribution of recently prepared virus in the host and is significant aim for stoping disease succession [6,7]. Peramivir a neuraminidase blocker showing the role of the viral neuraminidase protein, so stoping the virus from replicating by budding from the host cell has shown to have hinderance. In significance of this task, the developing of novel possible blockers against this enzyme might show new group of neuraminidase blocker. Therefore, the current examination objectives on virtual selection of neuraminidase blockers with a number of peramivir similar to compounds recovered from the ZINC database and docked arrangement of peramivir along with PASS calculation and ADME-Toxicity possibility.

Materials and Methodology

Protein structure

3D structure of neuraminidase of influenza virus was obtained from PDB (Protein Data Bank). Its PDB ID is 1NN2. The crystal configuration of neuraminidase of influenza virus

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made of two chains. We just used chain A for molecular docking in this study. All the water molecules and co-factor were also detached. We also removed the ligands which were already attached with the protein.

Ligand preparation

Three dimensional structure of ligand was obtained from PubChem (CID 151164). Then structure of analogs of ligands was retrieved from Zinc database. We also modified the original ligand by using Auto-Dock. Peramivir is the original ligand are and Aramivire, Munimivire, Anamivire are our modified ligands. Modifications are done by using Auto-Dock. Table 1 shows the replacement of elements done in original ligand.

Molecular docking

We performed molecular docking by utilizing Auto-Dock Vina. After the preparation of protein and ligands there PDBQT files were saved in the Vina folder. Then grid is made by opening the protein structure at Auto-dock. Grid cavity size is selected to bind the compounds. The bond elasticity of ligand was placed by making torsion in the ligands. Pay Mol is used to see the attraction among the substrate protein and the ligand [8] (Table 2).

ADME/Toxic prediction

ADMET properties are checked by using MED CHEM DESIGNER. It gives immediate contact to spectral and chemical databases, and foresees functions like physicochemical, ADME and toxicity properties [9]. Scoring was also carried out by using web-based service that is DSX-Online.

Results and Discussion

We downloaded the 3D structure of neuraminidase from PubChem Database. We have performed Molecular docking by autodock

The interactions between neuraminidase and first ligand aramivire can be seen in (Figure 1 a,b) and intreraction between second ligand munimivire and substrate protein can be seen in (Figure 2 a,b). Similarly attraction between third ligand anamivire and substratre protein is shown in (Figure 3 a,b). These pictures are taken from autodock vina to understand protein-ligand affinity.

Furthermore we have examined the pharmacological factors by means of ADME/Toxicity assessment that is revealed in Table 3, where it symbolizes the molecular mass, hydrogen bond donor and acceptor, and examined log p. From the ADME/Toxicity study, it is discovered that peak docked molecules have enhanced quantity of circulation, improved permeability and superior absorption rate in contrast to Peramivir (Table 4).

Table 1: Replacement of elements done in original ligand.

peramivir	H 39	C18	H45	N6	H38	H44	C11	C19	N7	H 29	H 47
Aramivire	O39	N18	C45	P6							
Munimivire								S19	O7		P47
Anamivire			C45		O38	N44	P11				

Table 2: Docking energies of different ligands.

Ligands	1	2	3	4	5	6	7	8	9
Peramivir	-6.7	-6.7	-6.7	-6.6	-6.6	-6.6	-6.5	-6.3	-6.2
Zinc 3981610	-6.1	-5.8	-5.8	-5.7	-5.6	-5.5	-5.5	-5.4	-5.4
Zinc 40709762	-6.6	-5.8	-5.8	-5.5	-5.5	-5.5	-5.4	-5.3	-5.2
Aramivire	-6.5	-6.2	-6.1	-6.1	-6.0	-5.8	-5.6	-5.6	-5.2
Munimivire	-6.5	-6.3	-6.2	-6.1	-6.0	-5.9	-5.9	-5.8	-5.6
Anamivire	-7.0	-6.9	-6.9	-6.9	-6.8	-6.8	-6.7	-6.7	-6.6

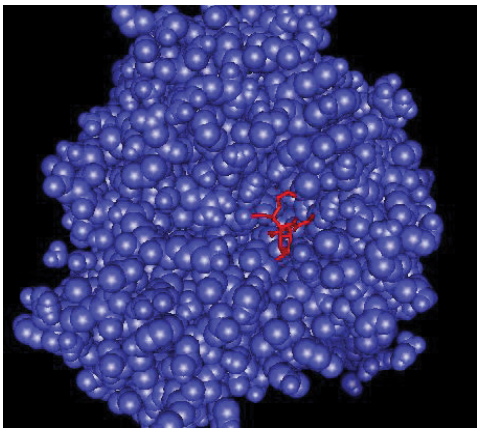

Figure 1a: Predicted bonded interaction between Aramivire with the Neuraminidase enzyme.

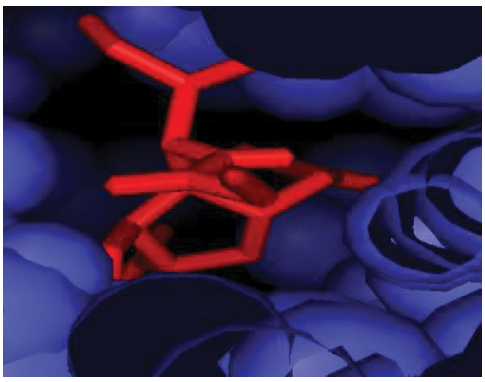

Figure 1b: Predicted bonded interaction between Aramivire with the Neuraminidase enzyme.

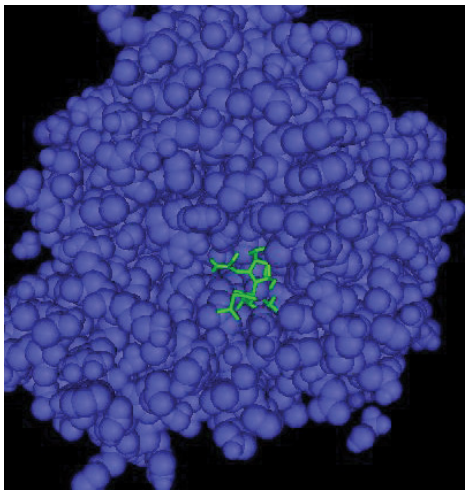

Figure 2a: Predicted bonded interaction between Munimivire and Neuraminidase.

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Conclusion

We have executed molecular docking examination and the molecular attraction analysis exposed that Anamivir have positive molecular interaction at the binding opening of the neuraminidase enzyme in contrast to Paramivir – an effective neuraminidase inhibitor. Best docking hits Aramivire, Munimivire and Anamivire utilized in this learning are a clear guide like molecule. Furthermore, ADME/Toxicity calculations exposed that Anamivire have improved pharmacological limits as compared to Paramivire too. So, we conclude that the molecular docking investigation and the ADME/Toxicity examination of Anamivire sustain experimental examination of these molecules to spot them as a major compound like Peramivir is informed to have hindrance against neuraminidase enzyme and bioavailability troubles.

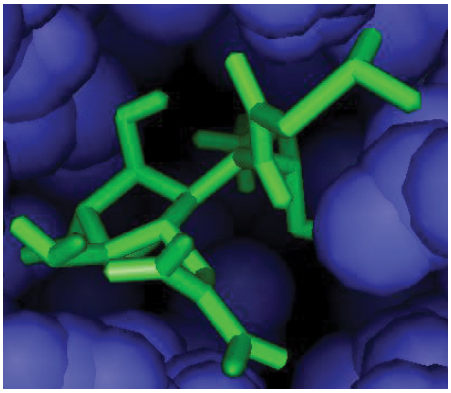

Figure 2b: Predicted bonded interaction between Munimivire and Neuraminidase.

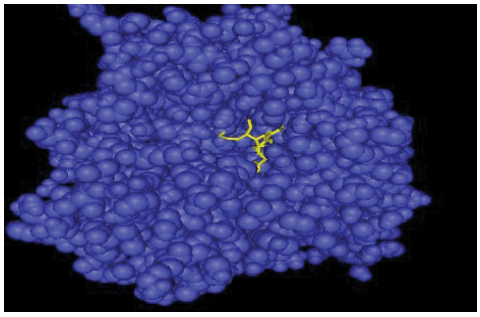

Figure 3a: Predicted attraction between Anamivire and neuraminidase.

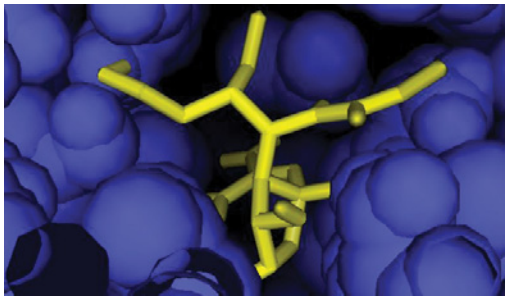

Figure 3b: Predicted attraction between Anamivire and neuraminidase.

Table 3: ADME/Toxicity prediction.

Ligands	MlogP	S+logP	S+logD	Rule of 5	Rule of 5 code	MWT	M-No	T-PSA	HBDH
Peramivir	-0.044	-1.449	-1.449	1.000	Hb	328.414	8.000	151.030	7.000
Zinc 3981610	-0.044	-1.449	-1.449	1.000	Hb	328.414	8.000	151.030	7.000
Zinc 40709762	-0.044	-1.624	-1.624	1.000	Hb	328.414	8.000	148.530	7.000
Aramivire	-0.280	-2.522	-3.158	1.000	Hb	378.411	9.000	165.300	9.000
Munimivire	-1.039	-2.632	-2.607	1.000	Hb	397.456	9.000	151.030	9.000
Anamivire	-0.792	-0.792	-1.675	1.000	Hb	391.410	I0.000	184.110	8.000

Table 4: Drug scoring.

Ligands	RMSD	Rank	Score
Peramivir	none	1	-67
Zinc3981610	none	1	-65
Zinc40709762	none	1	-58
Aramivire	none	1	-87
Munimivire	none	1	-71
Anamivire	none	1	-74

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