

In-Silico Analysis and Molecular Docking of Anti-HIV Drugs [Raltegravir and Rilpivirine] Against Integrase Enzyme and Reverse Transcriptase Enzyme of Human Immunodeficiency Virus

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Abstract

The 3D molecular structures and protein crystal structures were obtained from the PubChem database and the Protein Data Bank, respectively. After selecting compounds with a lower binding energy compared to the control medicines, SwissADME was used for pharmacokinetics screening. Six substituted derivatives of Raltegravir (RAL) drug and four substituted derivatives of Rilpivirine (RPV) drug were taken into account after thorough literature survey. The substituted derivatives of Raltegravir are abbreviated as RAL1, RAL2, RAL3, RAL4, RAL5 and RAL6 respectively. The substituted derivatives of Rilpivirine are abbreviated as RPV1, RPV2, RPV3 and RPV4 respectively. The Raltegravir derivatives were docked against the Integrase Enzyme with PDB ID 3OYA while the Rilpivirine derivatives were docked against the Reverse Transcriptase Enzyme with PDB ID 2ZD1. The docking score of RAL4 and RPV1 was found to be -8.3 and -8.7 kcal/mol correspondingly showing lower binding energies than the other derivatives which depicts stable ligand receptor complex. RAL4 shows higher affinity to the receptor than the original drug (RAL). Taking this into account ADME profile and 2D Interaction were carried out with the top scoring derivatives.

Compound	Binding energy [k/mol ⁻¹]	Rmsd Value Of Second Pose	
		Lower bound	Upper bound
RAL	-7.4	3.271	6.38
RAL 1	-6.7	2.601	6.849
RAL 2	-7.6	5.327	9.859
RAL 3	-7.9	3.373	4.537
RAL 4	-8.3	1.582	2.312
RAL 5	-7.9	1.902	2.6
RAL 6	-8.1	1.489	2.632

Binding energy of the Compound RAL

Compound	Binding energy [k\mol-1]	Rmsd Value Of Second Pose	
		Lower bound	Upper bound
RPV	-12 .6		
RPV1	-8.7	1.276	2.291
RPV2	-8.6	4.489	9.127
RPV3	-8.6	3.518	9.521
RPV4	-8.6	2.949	3.848

Binding energy of the Compound

Introduction

The WHO predicts that 39.9 million people will be living with HIV by the end of 2023, highlighting the gravity of this global public health concern. Around 630,000 individuals lost their lives in 2023 due to HIV/AIDS, and another 1.3 million individuals contracted virus for first time. More than two-thirds of the world's HIV-positive population resides in the WHO African Region, making it the region hit the worst. After many years of untreated HIV, the disease can escalate to AIDS. Adults and adolescents are now considered to have Advanced HIV Disease if their CD4 cell count is fewer than 200 cells/mm³ or if they are in WHO stages 3 or 4. Those under the age of five who are living with HIV are deemed to have advanced HIV illness. [1]

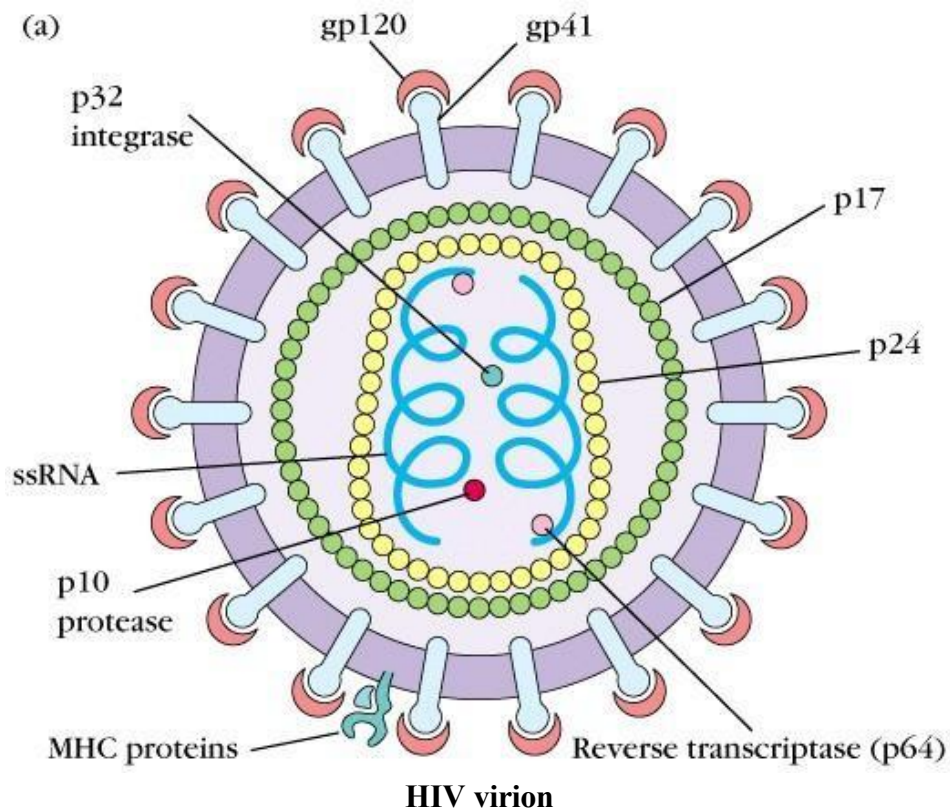
The symptoms of HIV might change as the illness progresses through its stages. The first three months after contracting HIV are the most contagious, yet many people don't find out they're HIV positive until much later. Symptoms may not appear for a few weeks following infection. Fever, headache, rash, and sore throat are symptoms that some people may have, similar to the flu. Lymph node swelling, decreased appetite, high body temperature, diarrhea, and cough are secondary symptoms.

Some of the physiological fluids that can transfer HIV from one person to another are breast milk, blood, sperm, and vaginal secretions. Pregnancy and delivery are additional routes of HIV transmission to a developing fetus.[2]

Rapid diagnostic testing can detect HIV and give results the very same day. This makes it much easier to detect health problems early and connect them to preventative and treatment measures. Additionally, HIV self-tests are available for individuals to utilize. Nevertheless, a comprehensive HIV positive diagnosis cannot be achieved with a single test; further testing, carried out via a competent and trained health professional is necessary. Using a nationally recognized testing approach and algorithm, prequalified tests from the World Health Organization may diagnose HIV infection with remarkable accuracy [3]

Detecting antibodies produced by an individual's immune response to combat HIV is the main focus of the most popular HIV diagnostic tests. Antibodies against HIV often develop in infected individuals within 28 days. During this so-called "window period," people can still infect others with HIV despite the fact that their antibody levels are so low that many rapid tests miss them. A second test can be administered after 28 days to those who have recently been exposed to a high-risk chemical and have tested negative the first time[4].

Fortunately, HIV may be avoided. The use of a condom, whether male or female, during sexual activity can prevent this. As a means of preventing HIV infection, doctors may prescribe antiretroviral medications (ARVs) containing dapivirine, and injectable long-acting cabotegravir[5].



Pathogenesis of HIV

The capacity of HIV to infect human cells with CD4 membrane receptors is crucial to its pathogenesis. A subset of T lymphocytes called helper/inducer or CD4 cells, together with monocytes, macrophages, and their hematologic progenitors, are major target cells. Depletion of CD4 cells is the direct cause of the immunodeficiency that is observed in late HIV illness. While physiologic and salutary relevance of these findings is fewer certain, further cell types that have been found to harbor HIV infection include epithelial gut cells, uterine cervical cells, and skin's Langerhans's cells [6].

CD4 receptors can bind to the gp41 envelope protein, which is linked to gp120 in a non-covalent manner (Fig. 2). As a result of this process, HIV can integrate into cell membranes. The virus sheds its envelope and releases its contents once it reaches the host cell's cytoplasm. The process of making DNA from the viral RNA template is known as reverse transcription. The newly synthesized viral DNA has two possible states: free floating or, as a provirus, incorporated into the cellular DNA by means of an endonuclease[7].

For an unknown duration, infected cells lie dormant. The pro-viral DNA begins to transcribe genomic and messenger RNA as soon as activation happens. Viral progenesis is regulated by the infected cell's activation state and the gene products mentioned before. New virions are formed once viral proteins are generated. They bud off of the infected cell and travel through the bloodstream, identifying new cells to infect. To further protect the newly generated viruses from neutralizing antibodies, infected cells might directly fuse with healthy CD4 lymphocytes[8].

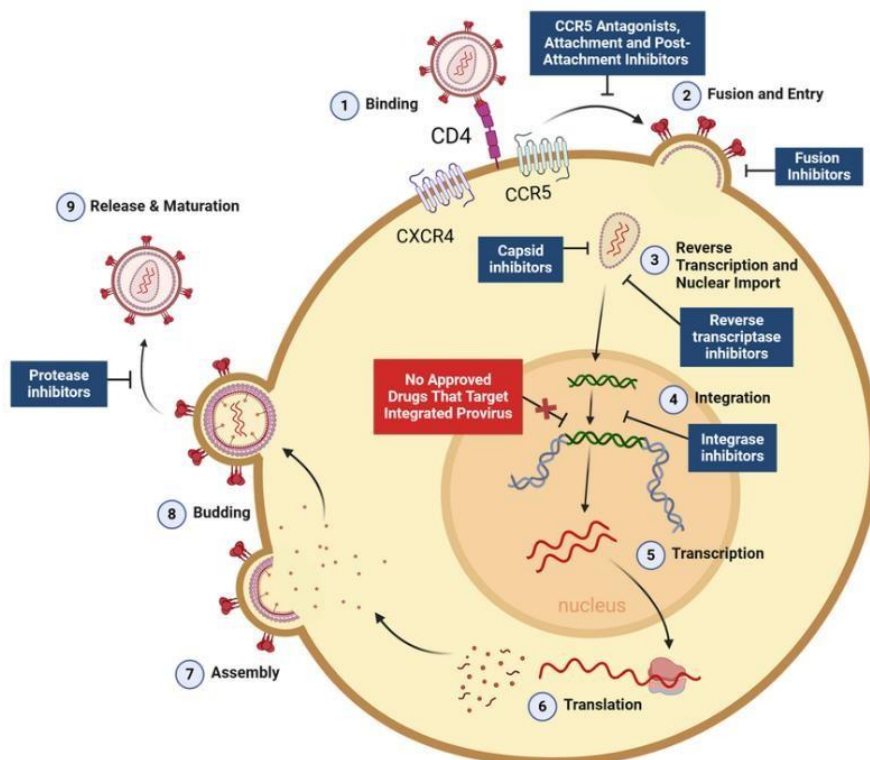
In the development of HIV infection, monocytes and macrophages play a significant role. The CD4 membrane receptor is the most common entry point for these cells during attachment. They seem to be tolerant to viral replication once infected, as they survive and spread the virus to different parts of the body. As a result, these cells are crucial for the production of newly protected viruses by the immune

system. It indicates that HIV infection partially inhibits monocyte and macrophage activity, which adds to immunosuppression[9].

CD4-T cells are the ones that HIV binds to. On CD4 receptors and two other coreceptors, CCR5 and CXCR4, the GP120 glycoprotein spikes and locks on. The viral membrane binds to the cell membrane as a consequence of this. The next process, reverse transcription, involves the viral enzyme reverse transcriptase converting viral RNA into complementary DNA (cDNA). There will be a lot of mutations because this method is prone to mistakes[10]. Cell machinery transform the viral RNA into viral DNA with two strands. The integrase enzyme binds to the viral DNA and transports it to the cell nucleus during the fourth phase, Integration.

The viral enzyme integrase integrates viral cDNA into host cell's DNA once it reaches nucleus. The infection becomes persistent due to this integration. HIV-stranded DNA either stays in the cell and replicates through the cell's machinery or stays dormant in the nucleus. This period is known as the LATENT PHASE [11]. Thus, the cell is referred to as latent. In these processes, transcription is the fifth step. The host's transcription machinery is utilized by the integrated viral DNA (provirus) to generate new viral RNA. In order to produce viral messenger RNA (mRNA) and viral genomic RNA, viral DNA utilizes host RNA polymerase[12].

The next step is the translation process. To construct viral proteins and enzymes, mRNA provides the necessary instructions. At the host cell membrane, the viral RNA and proteins assemble to produce immature virions, and then the newly created viruses exit the cell. A lipid sheath is acquired by the immature virions as they bud off the host cell membrane [13]. The viral proteins GP41 and GP120 are synthesized from lipids and fats found on the cell wall's surface. In order to create mature and infectious viral particles, viral proteases cut precursor proteins to create a capsid [14].



Pathogenesis of HIV

Molecular Formula: C₂₀H₂₁FN₆O₅

Chemical Name: *N*-[2-[4-[(4-fluorophenyl) methylcarbamoyl]-5-hydroxy-1-methyl-6-oxopyrimidin-2-yl] propan-2-yl]-5-methyl-1,3,4-oxadiazole-2-carboxamide

Developed in October 2007, the United States approved raltegravir, the first integrase inhibitor.[8,18,19] The Journal of Medicinal Chemistry published a study by Summa et al., detailing its development by Merck. In [20], The initial generic raltegravir medications were approved for use in July 2024 by the UK's MHPRA for HIV patients weighing 40 kg or more, whether they were adults or children. Lupin Healthcare (UK) Limited including Zentiva Pharma UK Limited were both given authorization[15].

Administration: Administer 400 mg film-coated tablet, two times daily for administration of adult individuals by HIV-1 infection.

Mechanism of Action: Raltegravir is an inhibitor of the retrovirus Integrase, which is essential for the HIV infection model because it prevents viral genetic material from being integrated into human chromosomes. In process of medication metabolism, glucuronidation is triggered.

An innovative class of antiretroviral medications, raltegravir blocks the HIV-1 IN. Antiretroviral therapy (ART) with raltegravir and other types of medicines was first authorized for use in individuals who had previously received treatment. For the treatment of HIV-1 infection, the USFDA has authorized use of raltegravir, first integrase inhibitor. In treatment-naïve and experienced individuals, raltegravir has been shown to be safe and efficacious in several clinical trials [16]. The side effects of Raltegravir-based therapy are less severe than those of older regimens. Among the suggested regimens for treating HIV-1 infection in patients who have not previously received any medication, Raltegravir has been included by the DHHS. Our study aims to address the growing problem of drug resistance in HIV-1 RT by developing and analyzing Raltegravir analogues using a throughput computational approach[17].

Since none of these medications kill the virus, they can only stop it from replicating, making HIV/AIDS an incurable disease. Inhibitors targeting new viral or cellular targets are always being sought after as a result of the unavoidable development of resistance to existing medicines[18].

Rilpivirine

Molecular Formula: C₂₂H₁₈N₆

Chemical Name: 4-[[4-[4-[(*E*)-2-cyanoethenyl]-2,6-dimethylanilino] pyrimidin-2-yl] amino] benzonitrile
Developed in April 2008, rilpivirine began phase III clinical studies; in May 2011, it was authorized for use in the US under the Edurant brand name.

Administration The medication can be taken orally (under the brand name Edurant) or intramuscularly (Rekambys) once monthly or every two months for a longer-lasting effect. To evaluate tolerance, the pills are taken for four weeks prior to injecting[19].

Mechanism of Action Rilpivirine is a non-competitive NNRTI that binds to reverse transcriptase. It inhibits the replication of HIV-1 and other RNA-dependent proteins by binding to DNA polymerase. It does not affect the action of human DNA polymerases α , β , and γ . Adaptability to changes in its non-nucleoside RT binding pocket makes rilpivirine less sensitive to modifications that induce resistance in viruses. This is due to its malleable structure around its aromatic rings[20].

Rilpivirine is a Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI) which is approved for treatment of HIV-1 infection in antiretroviral-naïve adult patients. Rilpivirine acts at the hydrophobic position near the NNRTI-binding site, resulting in inactivation of the HIV-1 RT and terminating the HPV DNA synthesis[21]. Rilpivirine was selected for further study due to this compound is able to bind and inhibit

the wild type of HIV-1 RT and a number of clinically relevant NNRTI-resistant variants. This ability derives from the geometrical flexibility of the compound within the HIV-1 RT binding pocket. Further investigation of the Rilpivirine shows a crucial role due to its activity against a wide range of drug-resistant variants[22]. Therefore, it plays an important role in highly active antiretroviral therapy (HARRT). In our study, we utilize throughout computational approach to design and analyse Rilpivirine analogues to overcome the rapid emergence of different types of strain mutations which lead to drug resistance by HIV-1 RT[23].

Observations

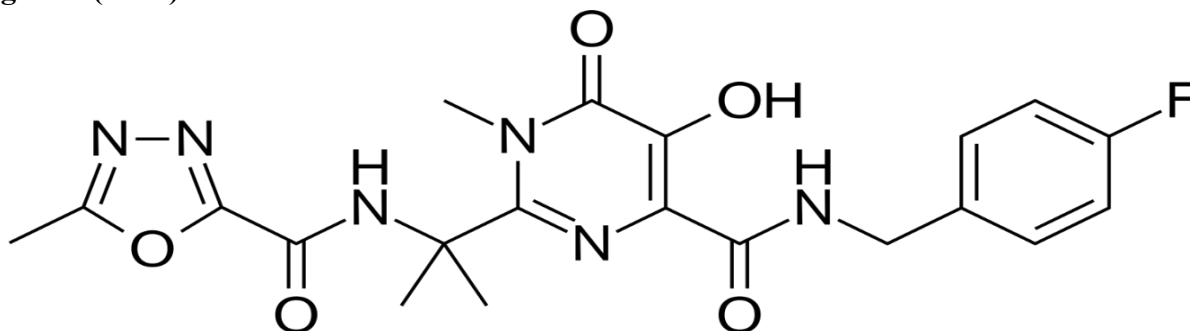


Uncleaned Protein 3OYA [IN]



Cleaned Protein 3OYA [IN]

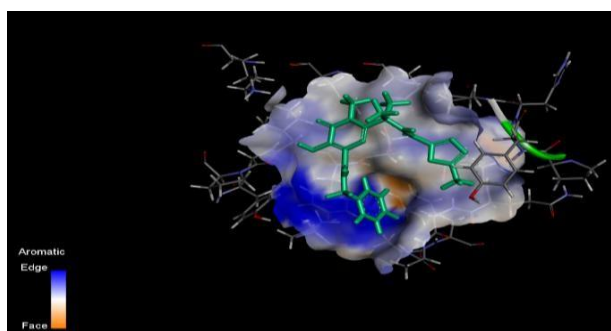
Raltegravir (RAL)



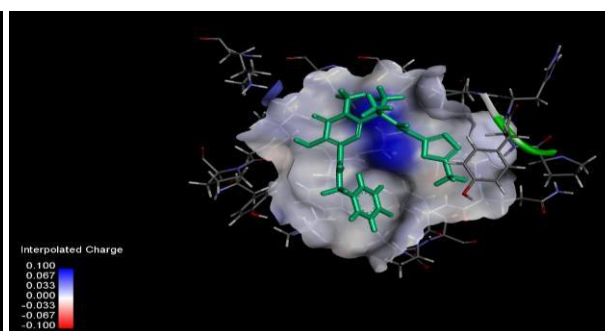
3D Molecular Structure of RAL

S	Score	RMSD l.b.	RMSD u.b.
V	-7.7	0.0	0.0
V	-7.4	3.271	6.38
V	-7.4	4.216	6.512
V	-7.4	1.843	2.386
V	-7.4	3.348	6.03
V	-7.3	3.364	7.636
V	-7.0	2.466	3.787
V	-7.0	3.34	7.005
V	-7.0	4.385	8.369
V	-7.0	3.291	5.476

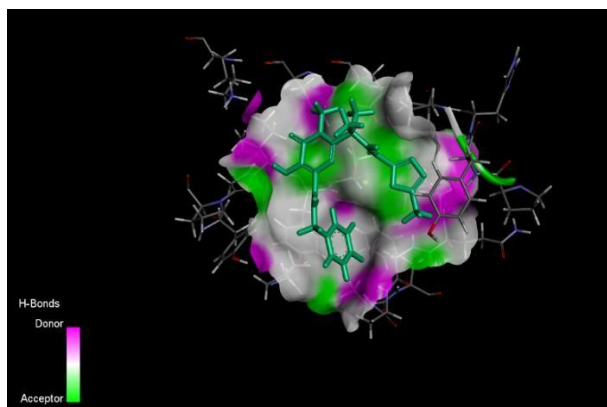
RAL Dockscore



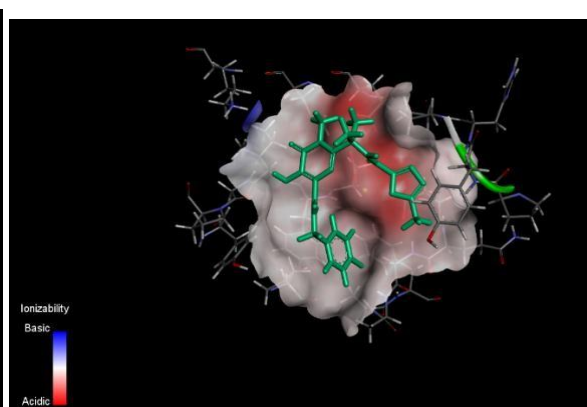
Aromatic Interaction



Interpolated charge interaction

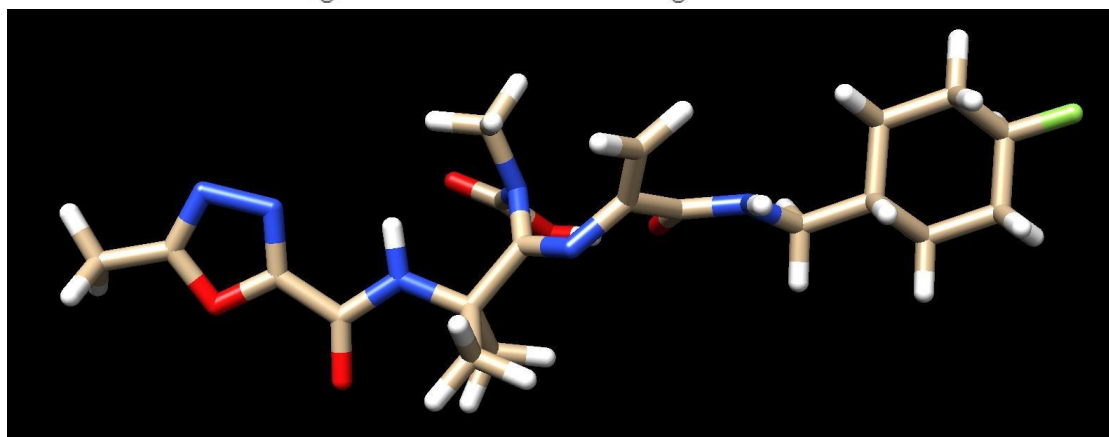
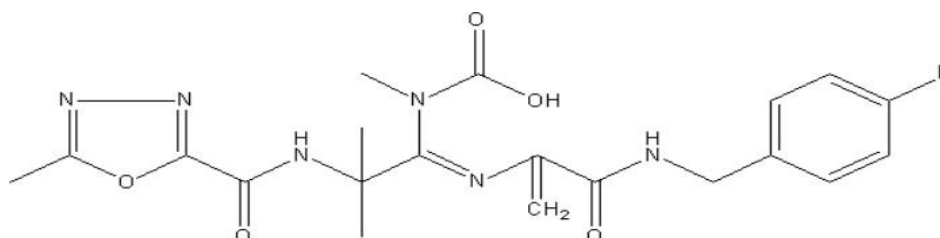


Sas Interaction



Ionizability interaction

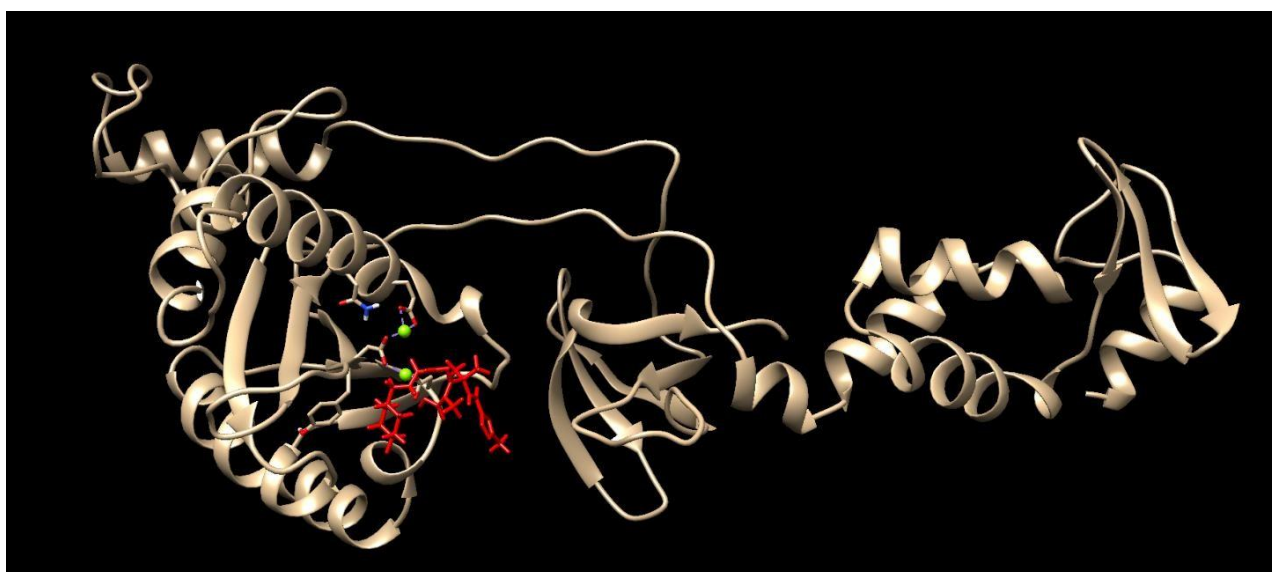
Raltegravir 1 (RAL1)



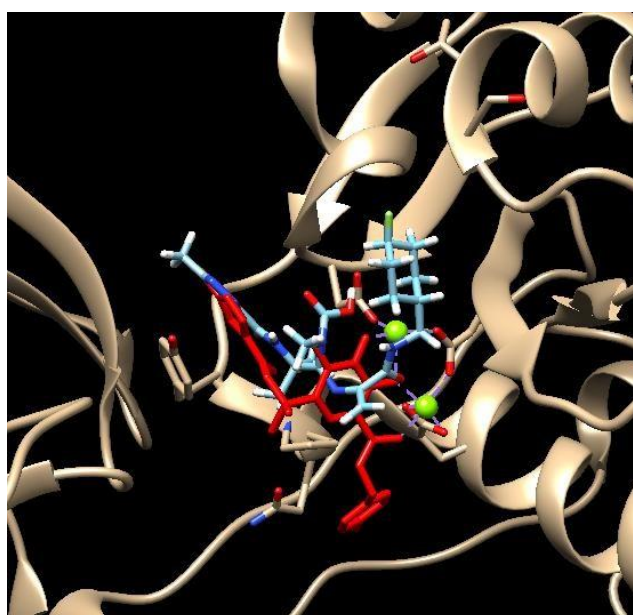
RAL1 3D

S	Score	RMSD l.b.	RMSD u.b.
V	-7.0	0.0	0.0
V	-6.7	2.601	6.849
V	-6.7	1.6	1.913
V	-6.5	1.029	1.395
V	-6.5	3.696	6.625
V	-6.4	3.338	7.089
V	-6.4	3.547	7.38
V	-6.3	3.897	5.264
V	-6.3	2.745	5.375
V	-6.3	2.564	3.691

RAL1 Dockscore

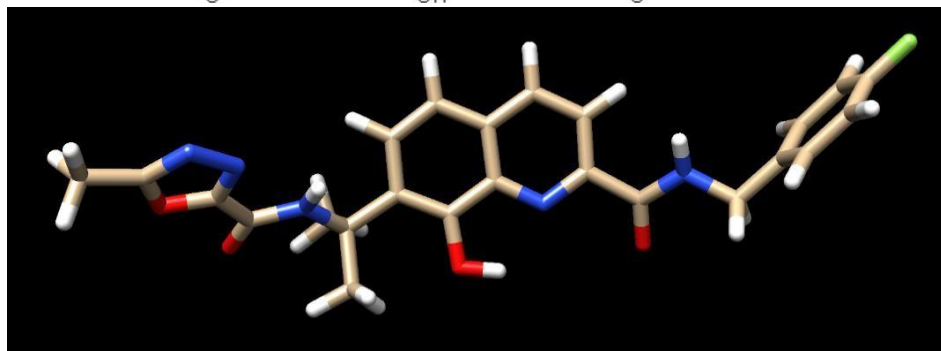
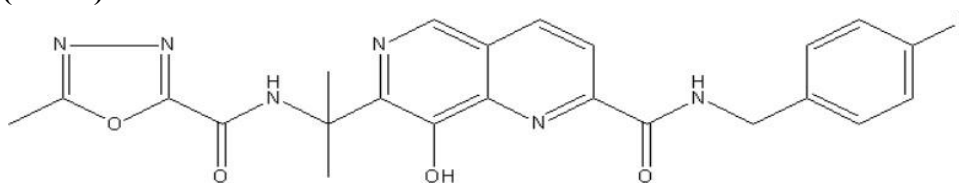


RAL1 against 3OYA [IN]



RAL and RAL1

Raltegravir 2 (RAL2)



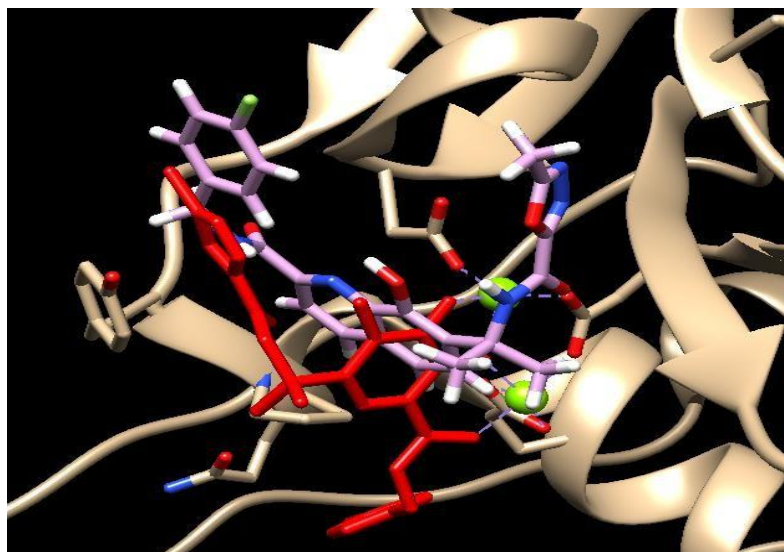
RAL2 3D

S	Score	RMSD l.b.	RMSD u.b.
V	-7.9	0.0	0.0
V	-7.6	5.327	9.859
V	-7.3	5.521	9.261
V	-7.2	5.826	9.508
V	-6.9	6.396	10.737
V	-6.9	5.896	10.396
V	-6.8	6.049	10.013
V	-6.7	5.389	9.744
V	-6.6	4.883	10.163
V	-6.5	5.008	9.283

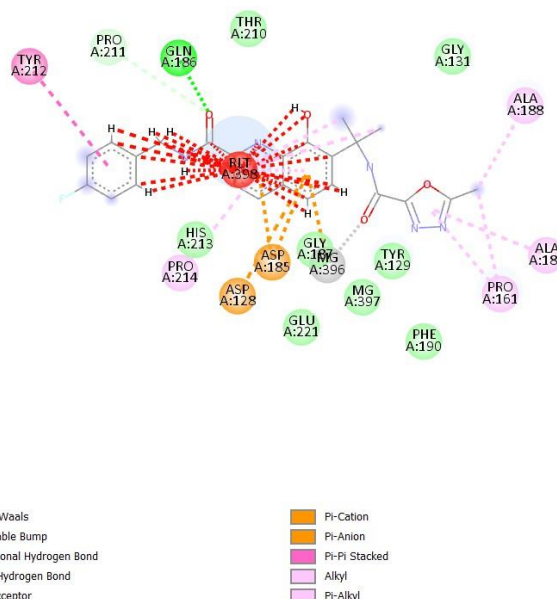
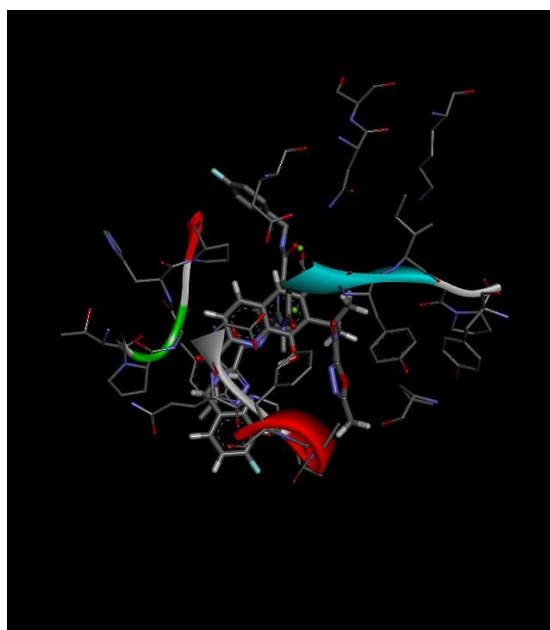
Dockscore of RAL2



RAL2 against 3OYA [IN]

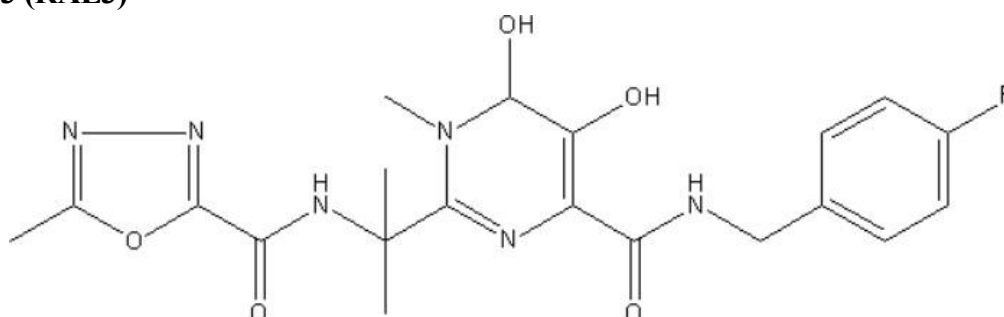


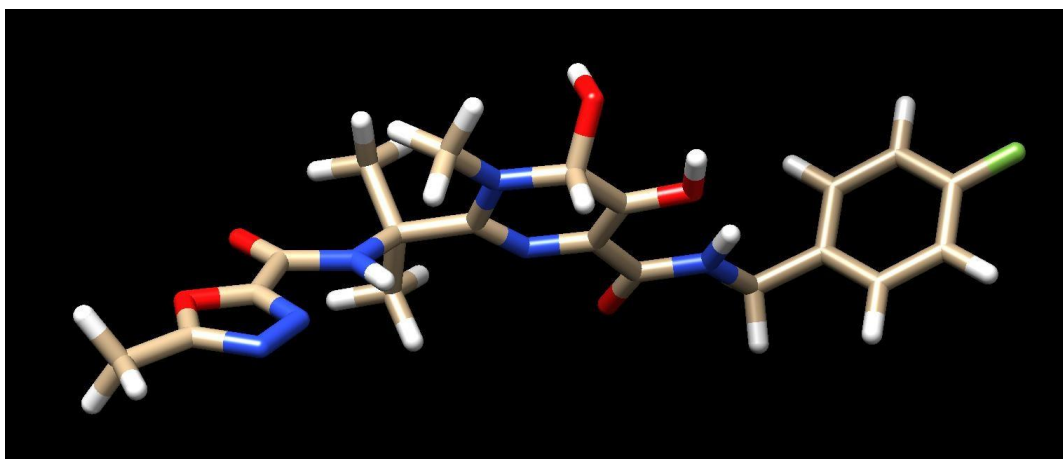
RAL and RAL2



RAL2 2D Interaction

Raltegravir 3 (RAL3)

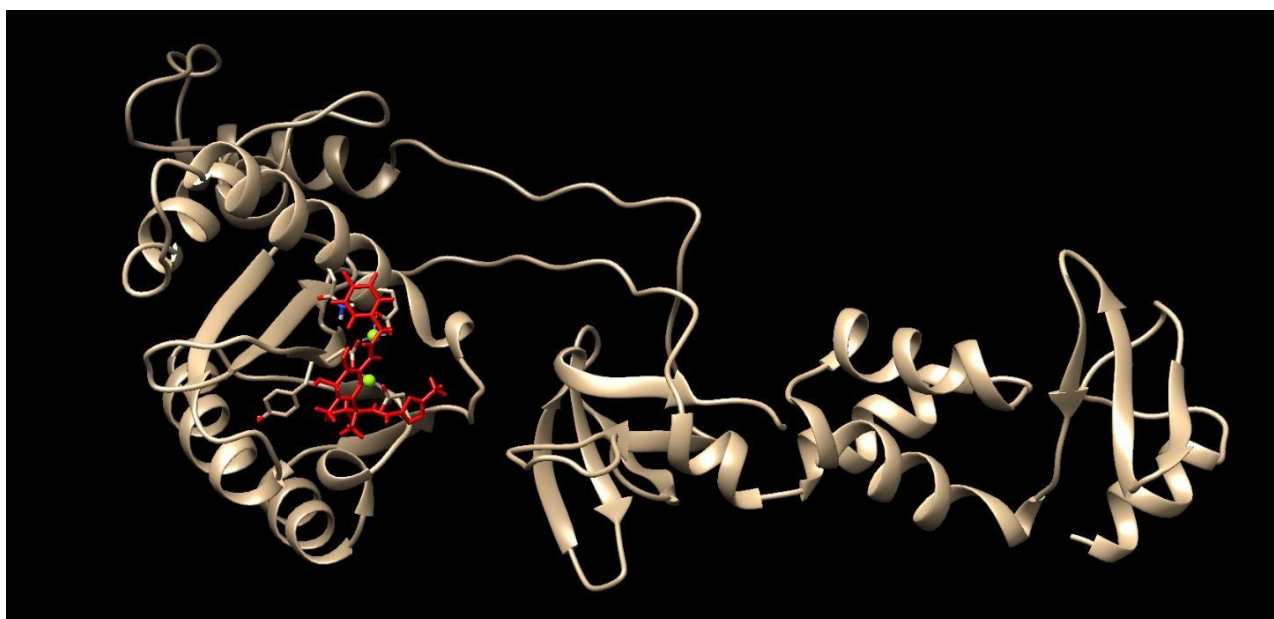




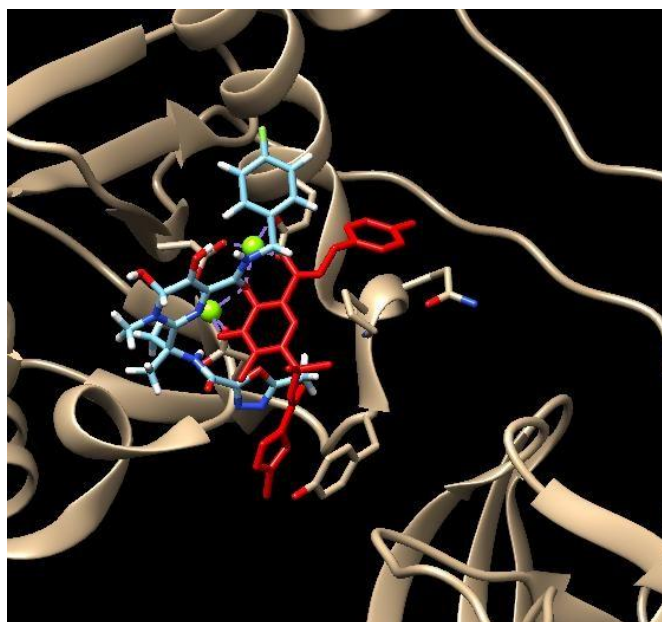
RAL3 3D

S	Score	RMSD l.b.	RMSD u.b.
V	-8.3	0.0	0.0
V	-7.9	3.373	4.537
V	-7.8	4.243	7.029
V	-7.5	4.106	5.865
V	-7.3	4.721	9.234
V	-7.3	2.625	4.632
V	-7.3	3.906	4.935
V	-7.2	4.171	8.274
V	-7.1	2.14	3.266
V	-7.0	4.512	8.556

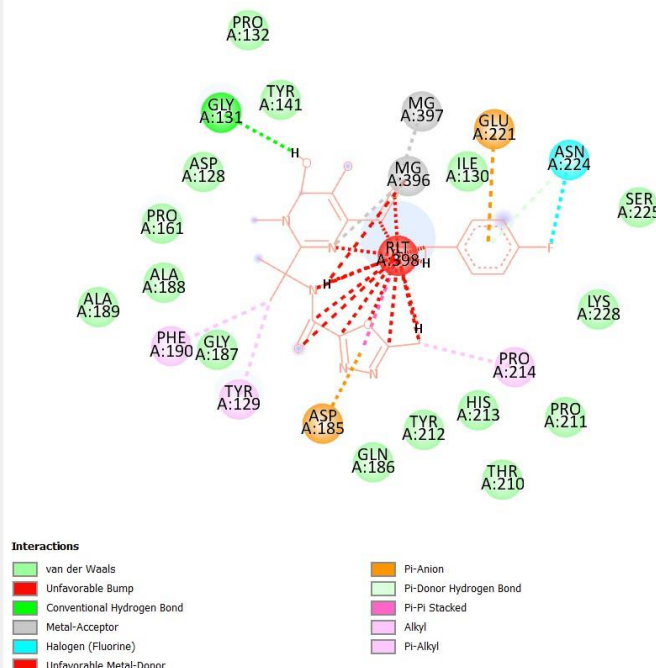
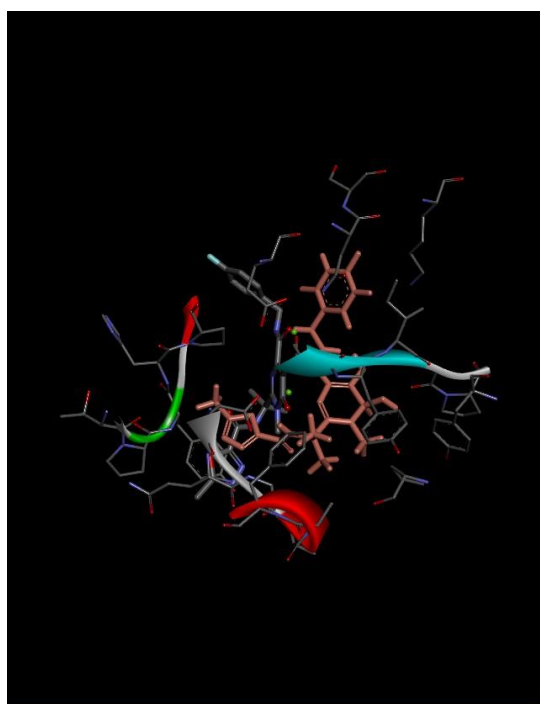
Dockscore of RAL3



RAL3 against 3OYA [IN]

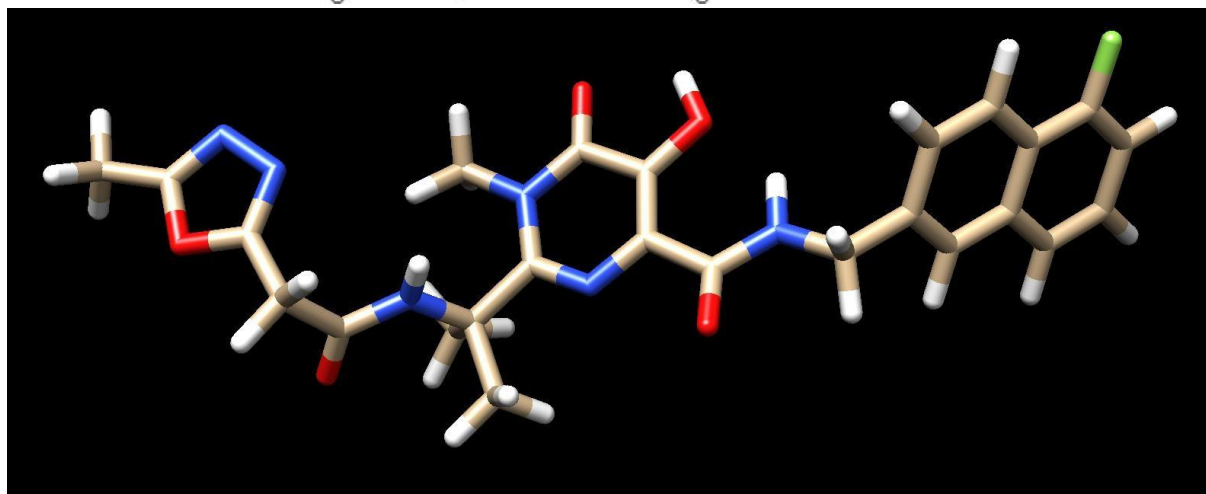
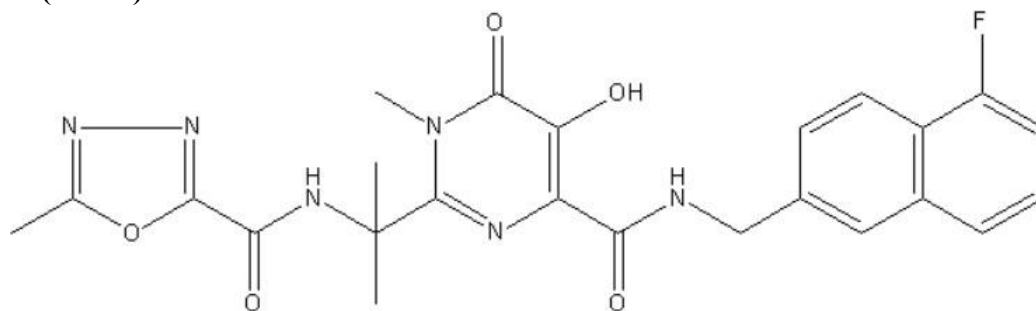


RAL and RAL3



RAL3 2D Interaction

Raltegravir 4 (RAL4)



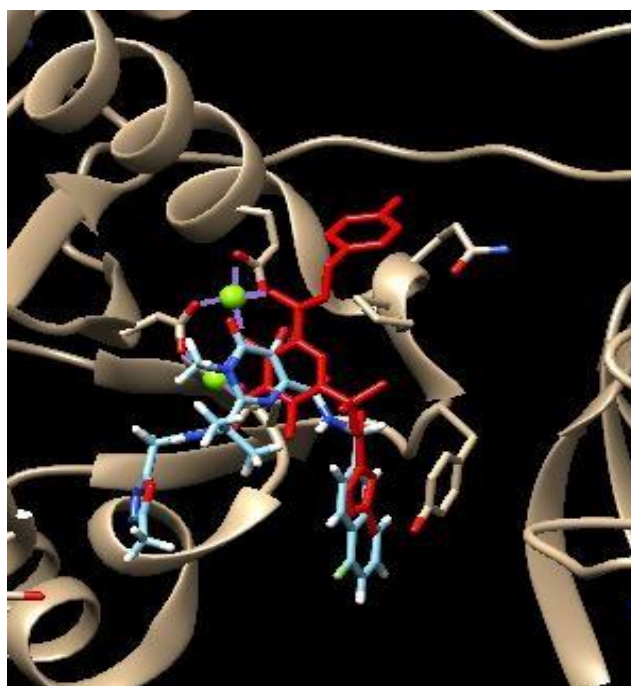
RAL-4 3D

S	Score	RMSD l.b.	RMSD u.b.
V	-8.3	0.0	0.0
V	-8.3	1.582	2.312
V	-8.2	2.992	5.34
V	-8.1	3.251	6.616
V	-8.0	4.478	9.378
V	-7.9	4.705	8.254
V	-7.7	4.606	9.065
V	-7.6	3.24	6.377
V	-7.6	3.488	7.211
V	-7.5	4.388	8.465

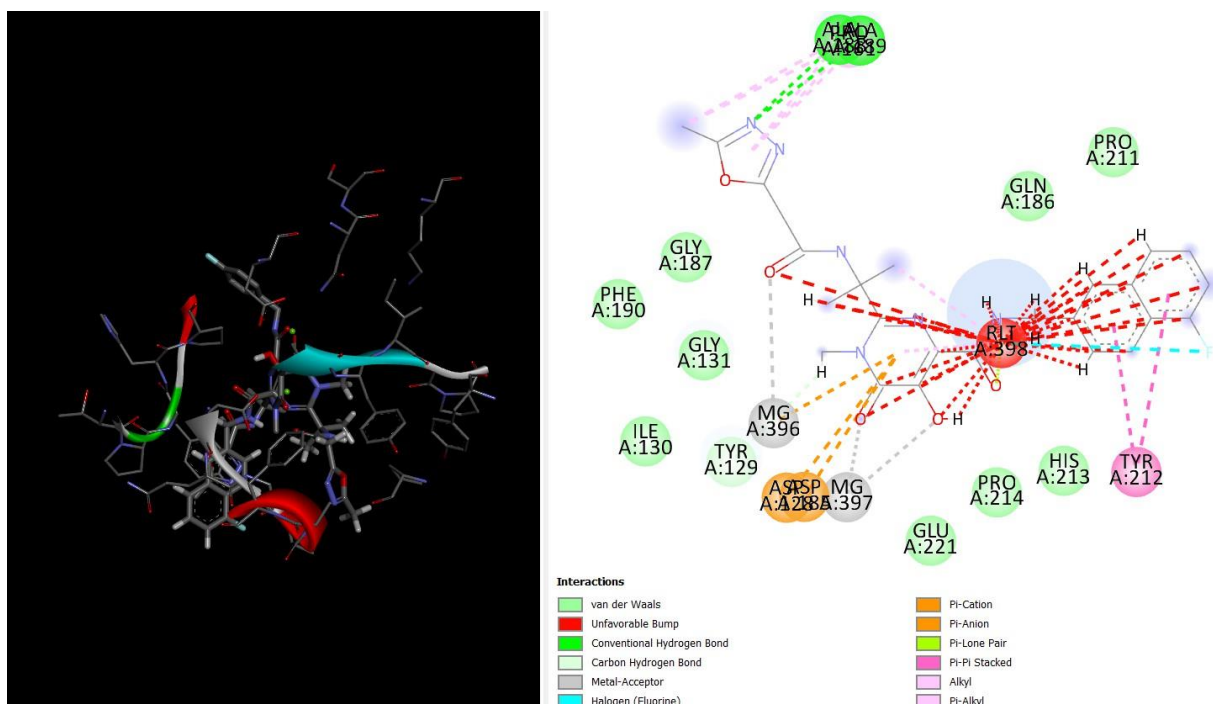
Dockscore of RAL4



RAL4 against 3OYA [IN]

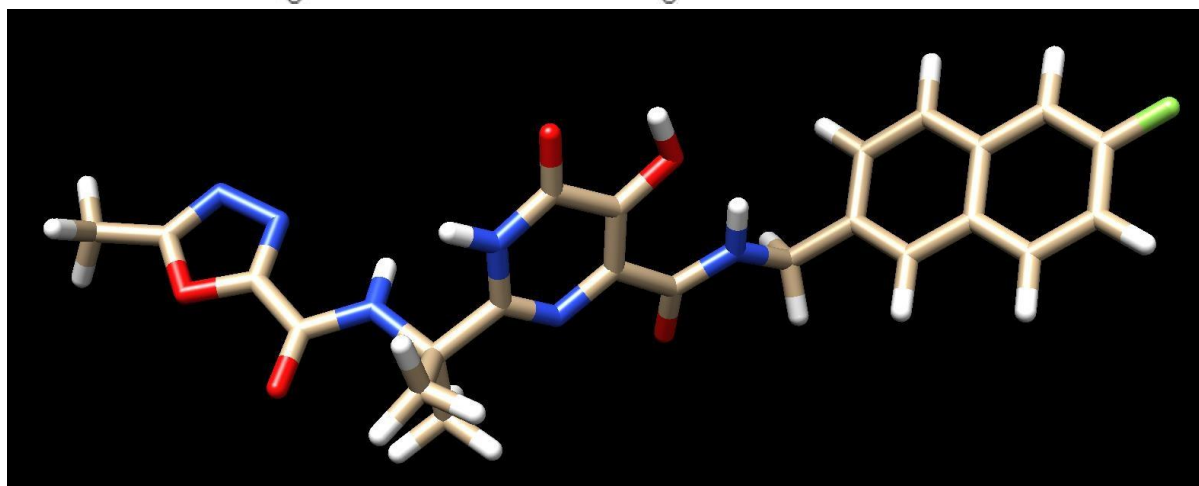
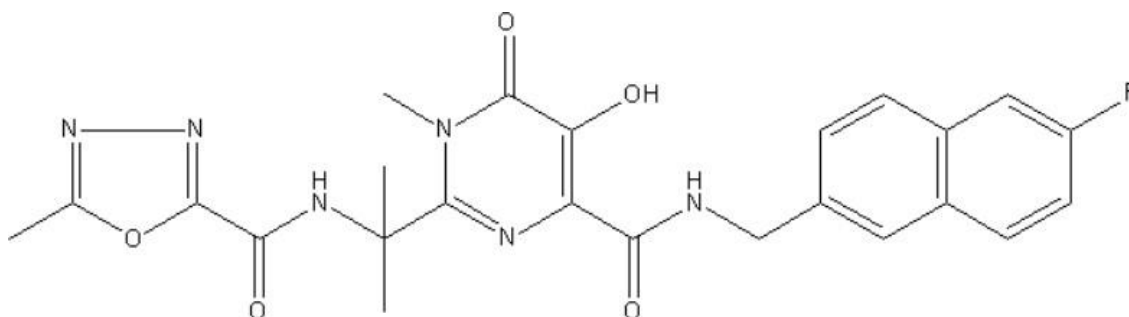


RAL and RAL4



RAL4 2D Interaction

RALTEGRAVIR 5 (RAL5)



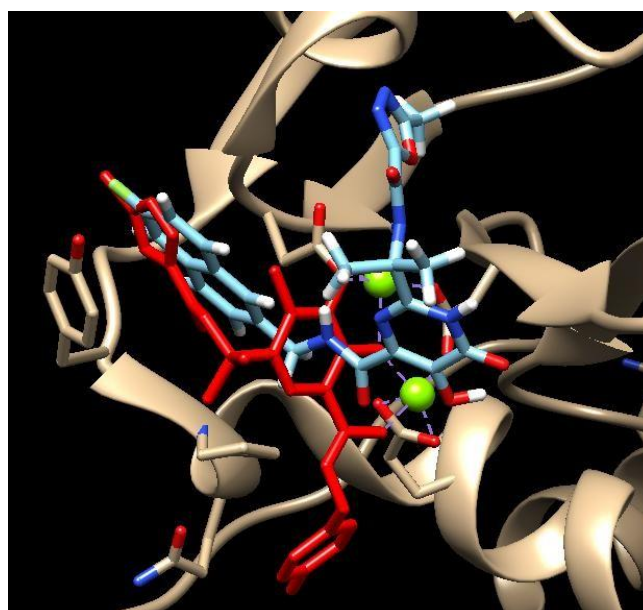
RAL5 3D

S	Score	RMSD l.b.	RMSD u.b.
V	-8.0	0.0	0.0
V	-7.9	1.902	2.6
V	-7.9	1.737	2.854
V	-7.8	3.547	6.887
V	-7.7	1.616	2.395
V	-7.7	2.435	5.956
V	-7.6	3.261	6.593
V	-7.6	2.268	3.143
V	-7.6	4.589	8.861
V	-7.5	4.975	9.023

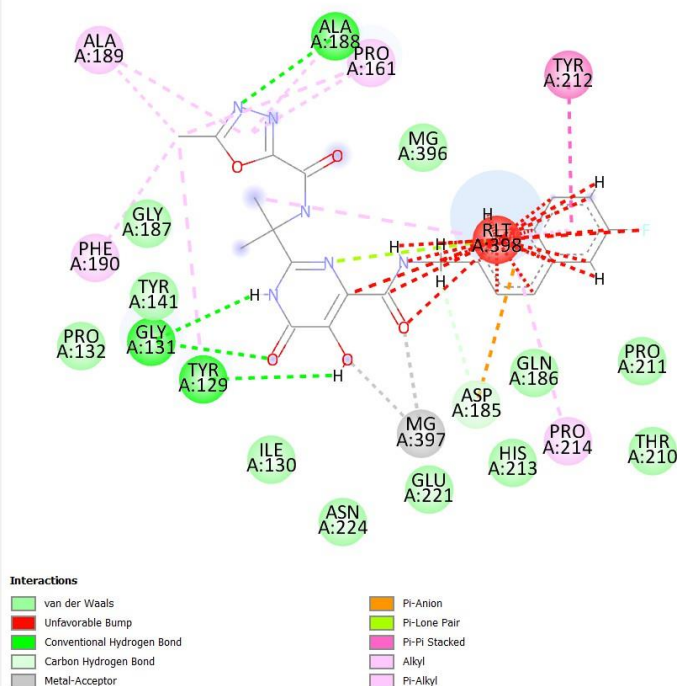
Dockscore of RAL5



RAL5 against 3OYA [IN]

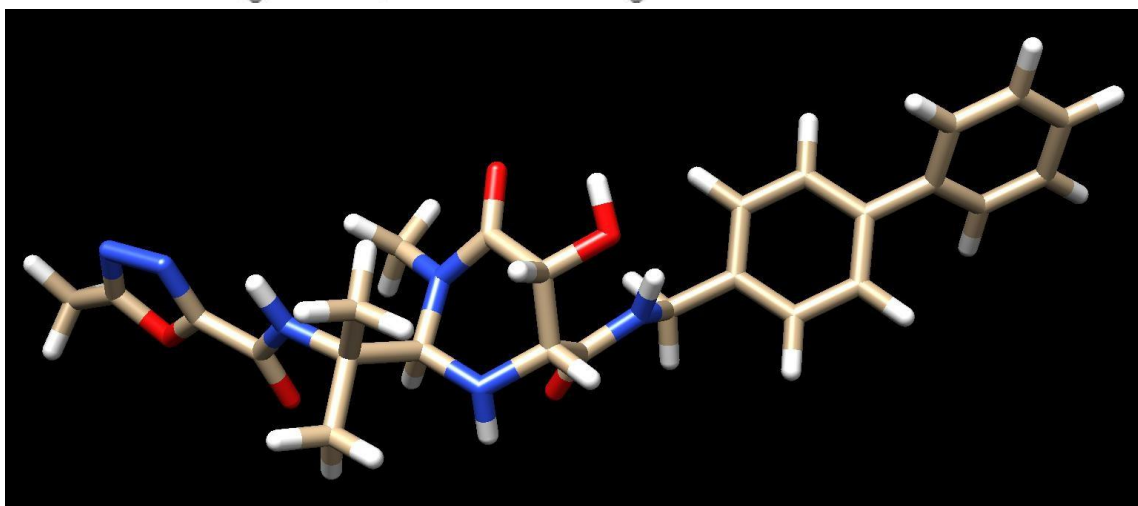
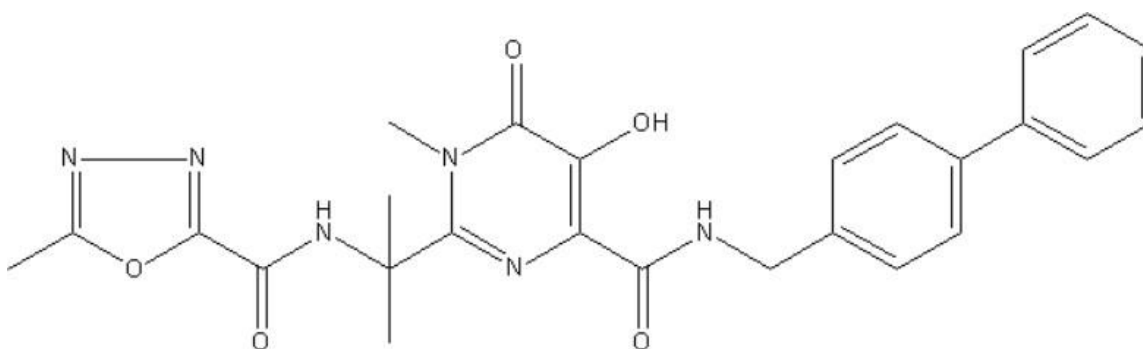


RAL and RAL5



RAL5 2D Interaction

Raltegravir-6 (RAL6)



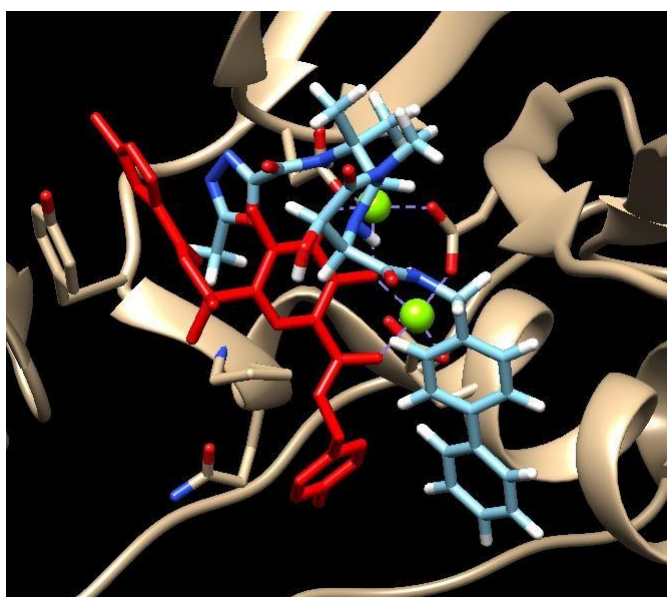
RAL-6 3D

S	Score	RMSD l.b.	RMSD u.b.
V	-8.1	0.0	0.0
V	-8.1	1.489	2.632
V	-7.6	1.912	3.094
V	-7.4	3.979	8.778
V	-7.4	2.026	3.379
V	-7.0	2.99	7.715
V	-7.0	2.373	3.894
V	-6.9	2.666	4.791
V	-6.8	3.109	4.613
V	-6.8	3.494	10.351

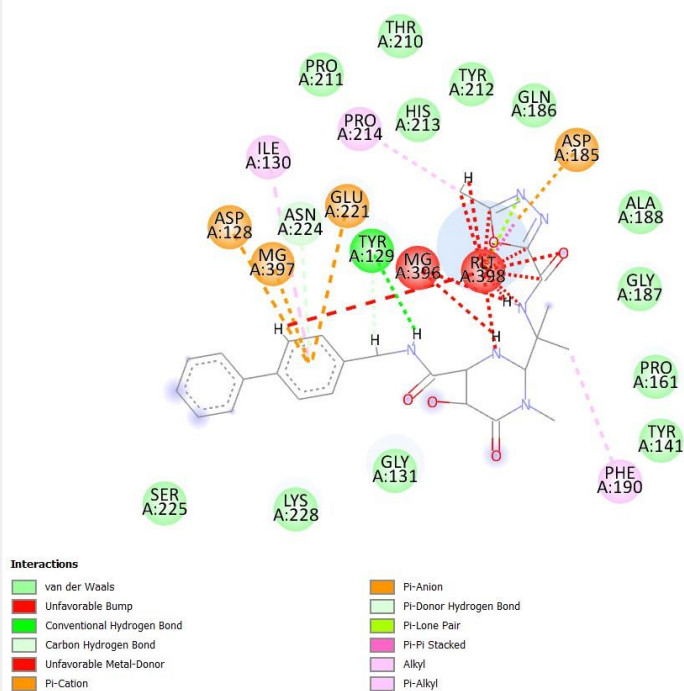
Dockscore of RAL-6



RAL-6 against 3OYA [IN]

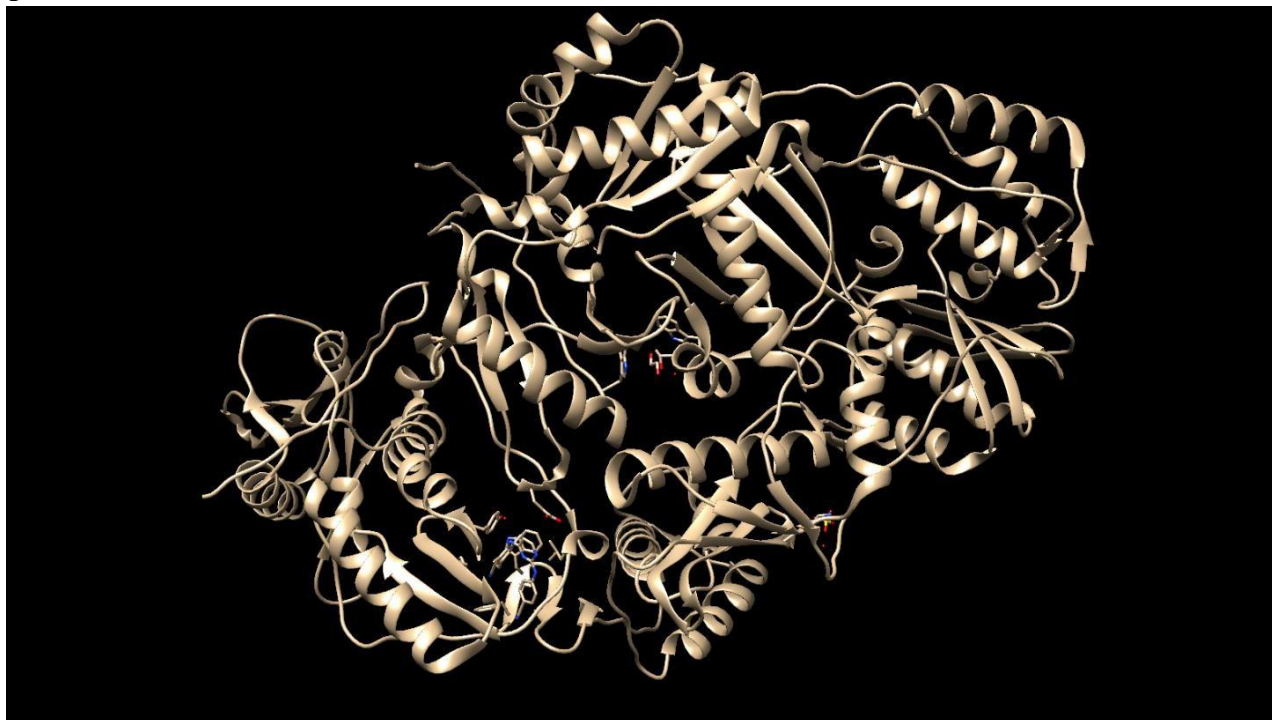


RAL and RAL-6

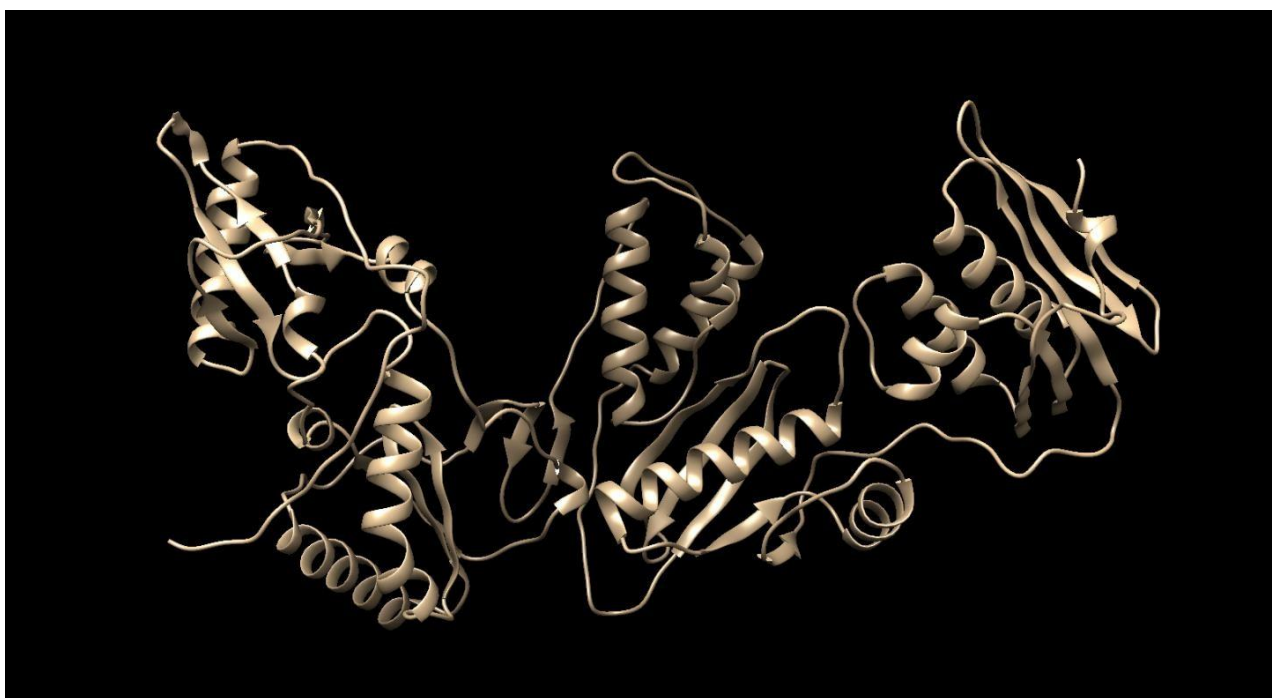


RAL-6 2D Interaction

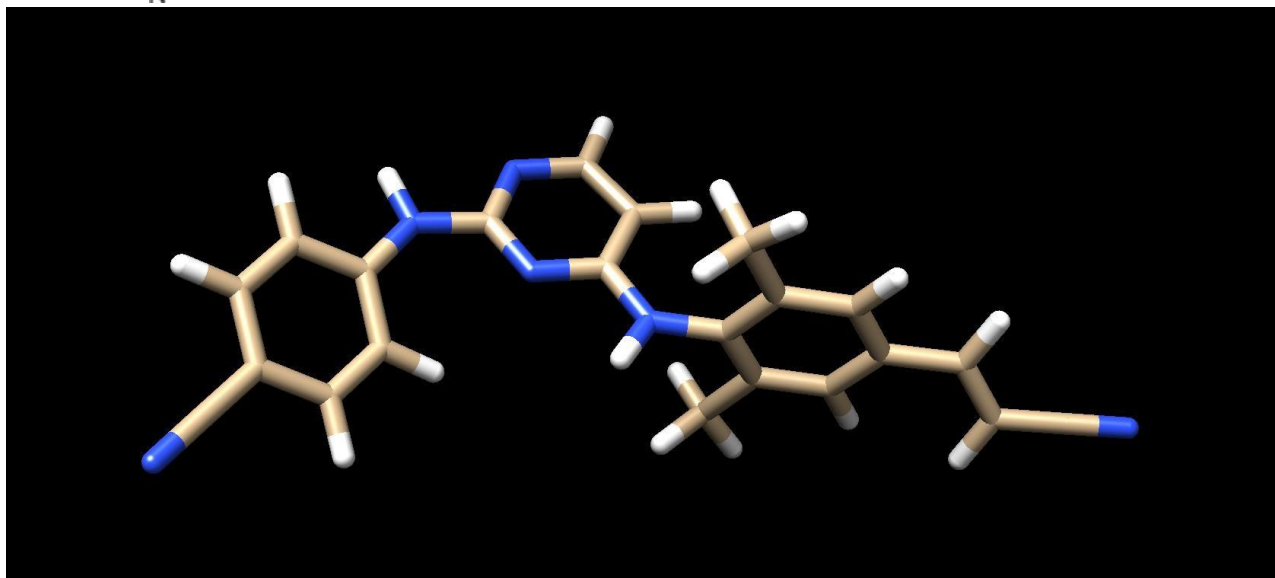
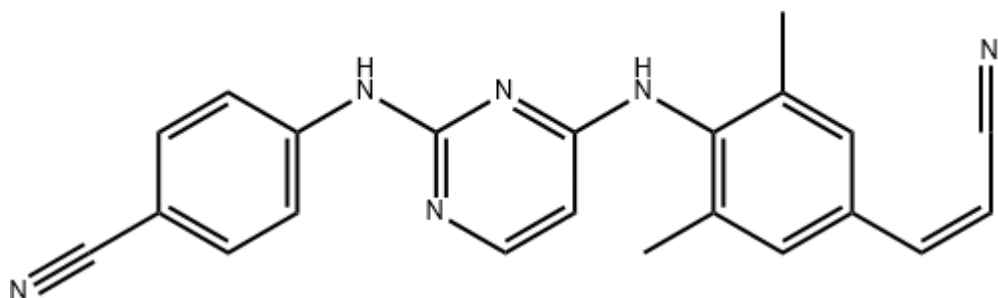
Rilpivirine



Uncleaned Protein 2ZD1 [RT]



Cleaned Protein 2ZD1 [RT]



RPV 3D Structure

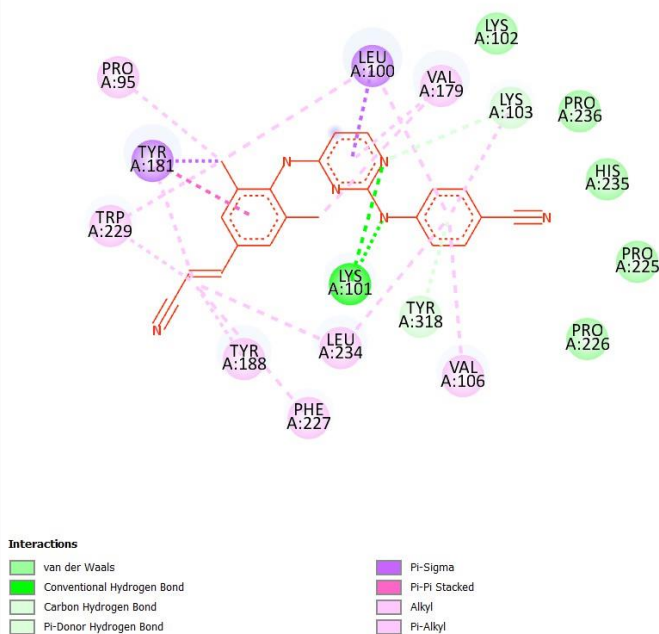
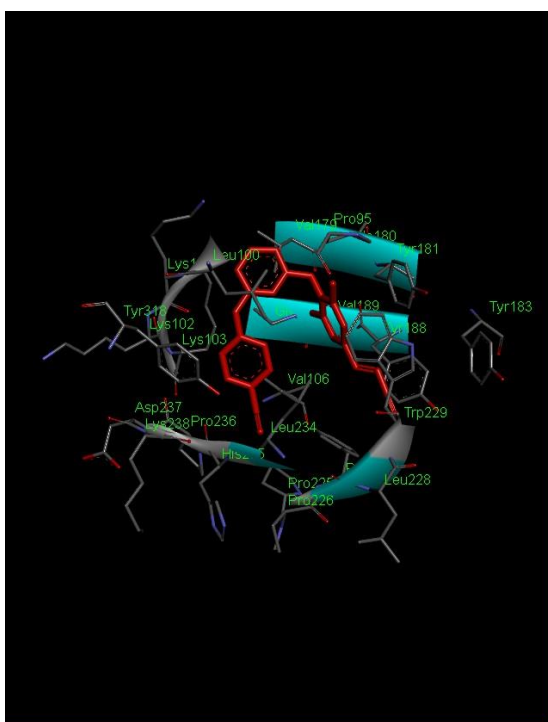
RPV 3D Structure

S	Score	RMSD l.b.	RMSD u.b.
V	-12.6	0.0	0.0

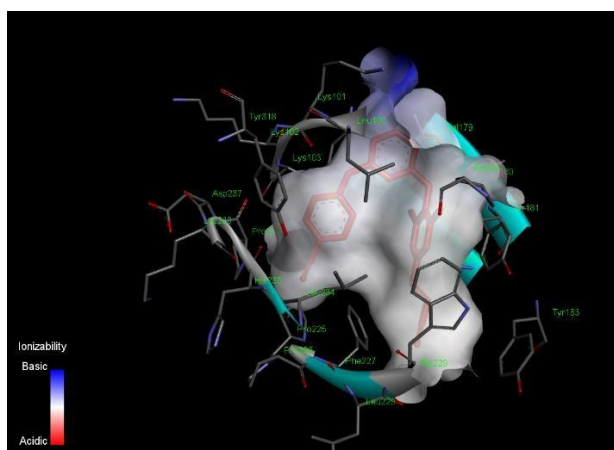
Dockscore of RPV



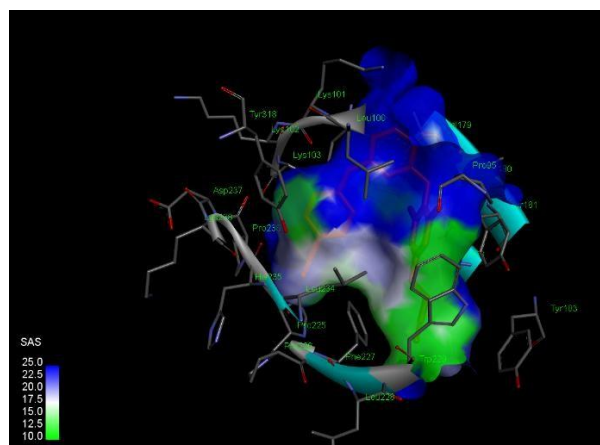
RPV against 2ZD1 [RT]



RPV 2D Interaction

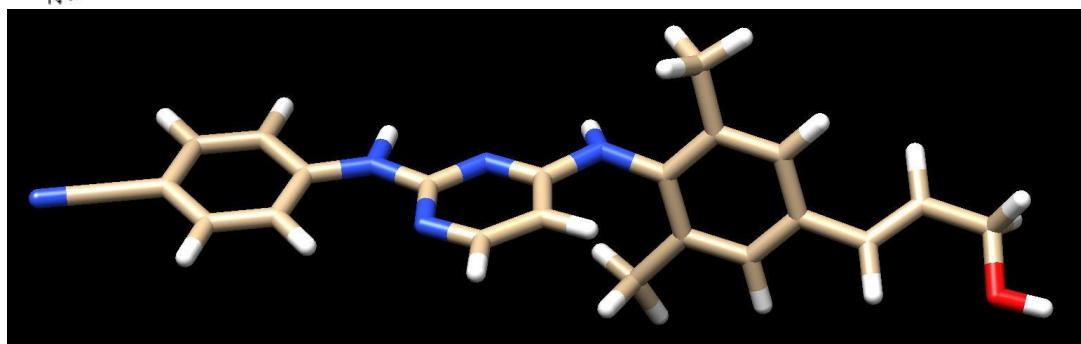
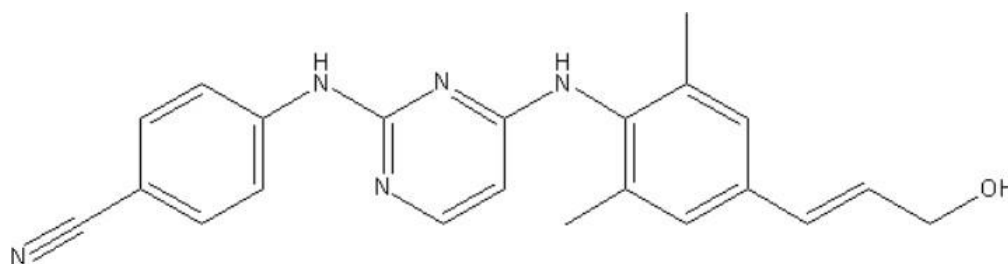


Ionizability interaction



SAS Interaction

Rilpivirine 1 (RPV1)



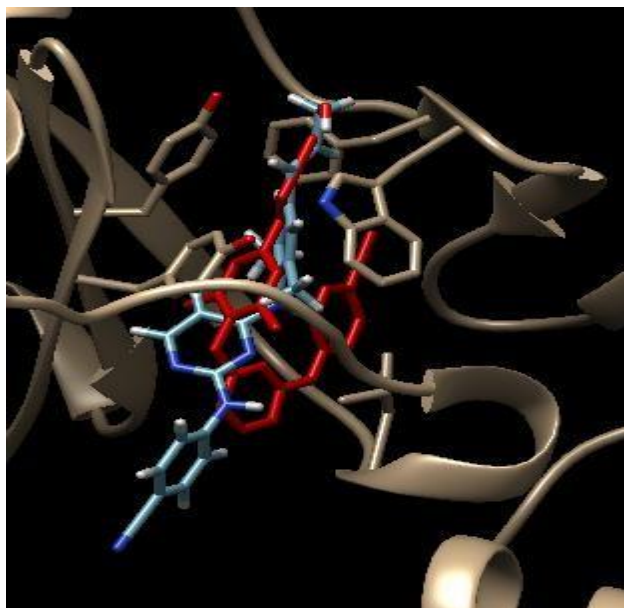
RPV1 3D

S	Score	RMSD l.b.	RMSD u.b.
V	-8.7	0.0	0.0
V	-8.6	1.276	2.291
V	-8.5	4.53	9.554
V	-7.9	4.902	10.355
V	-7.8	4.941	10.311
V	-7.7	4.778	10.123
V	-7.6	4.213	10.842
V	-7.5	4.099	10.142
V	-7.5	4.056	8.758
V	-7.5	4.302	8.873

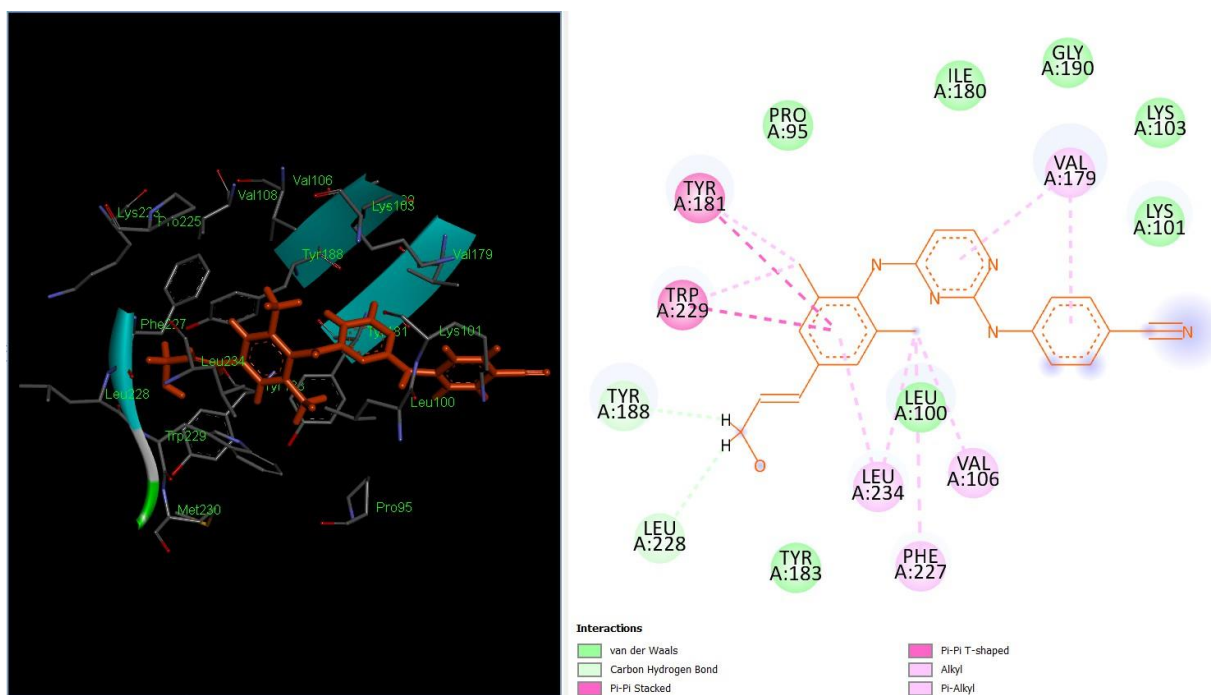
Dockscore of RPV1



RPV1 against 2ZD1 [RT]

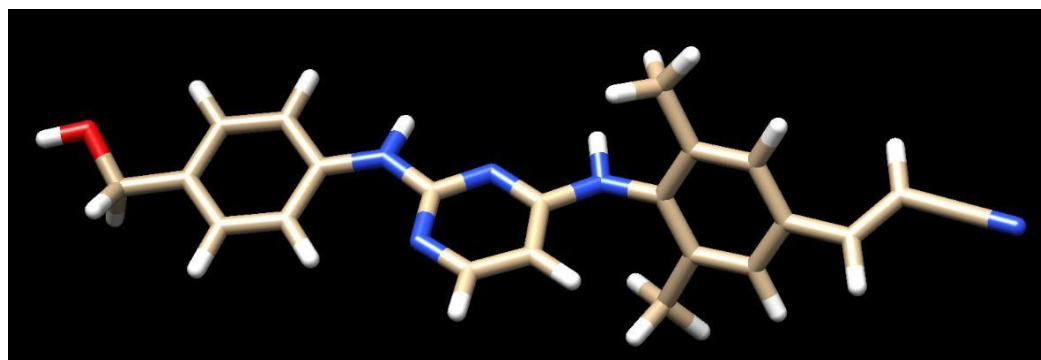
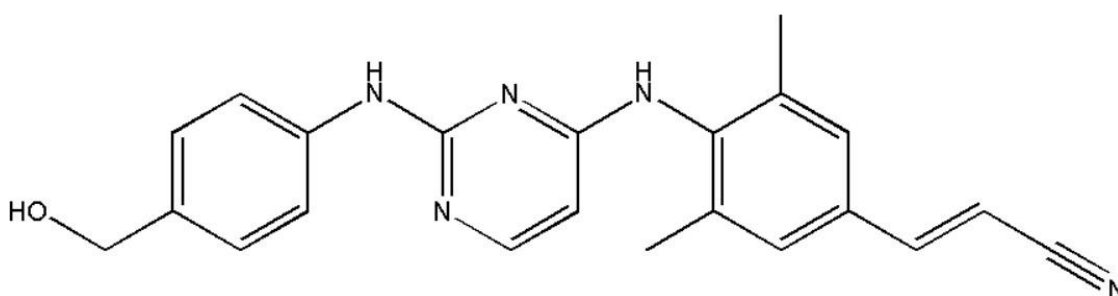


RPV and RPV1



RPV1 2D Interaction

Rilpivirine 2 (RPV2)



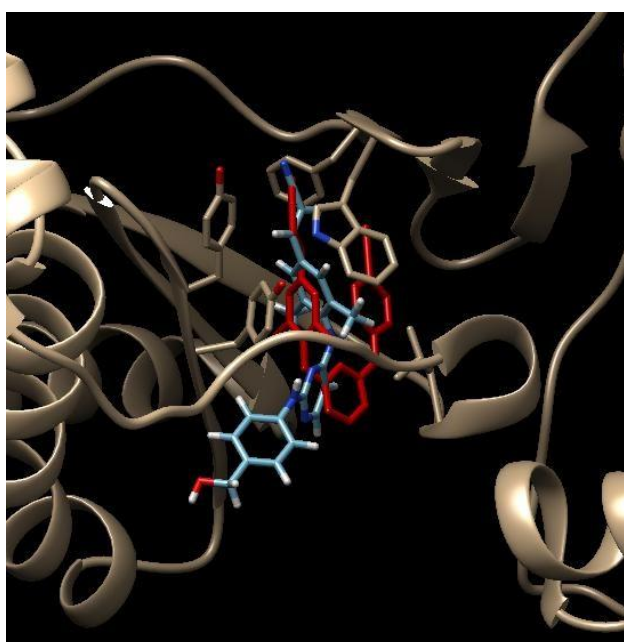
RPV2 3D

S	Score	RMSD l.b.	RMSD u.b.
V	-8.6	0.0	0.0
V	-8.1	4.489	9.127
V	-8.0	4.065	9.191
V	-8.0	4.521	9.045
V	-7.8	3.969	8.924
V	-7.8	2.721	4.04
V	-7.6	4.493	9.289
V	-7.5	4.1	10.002
V	-7.5	4.155	9.451
V	-7.4	4.361	9.251

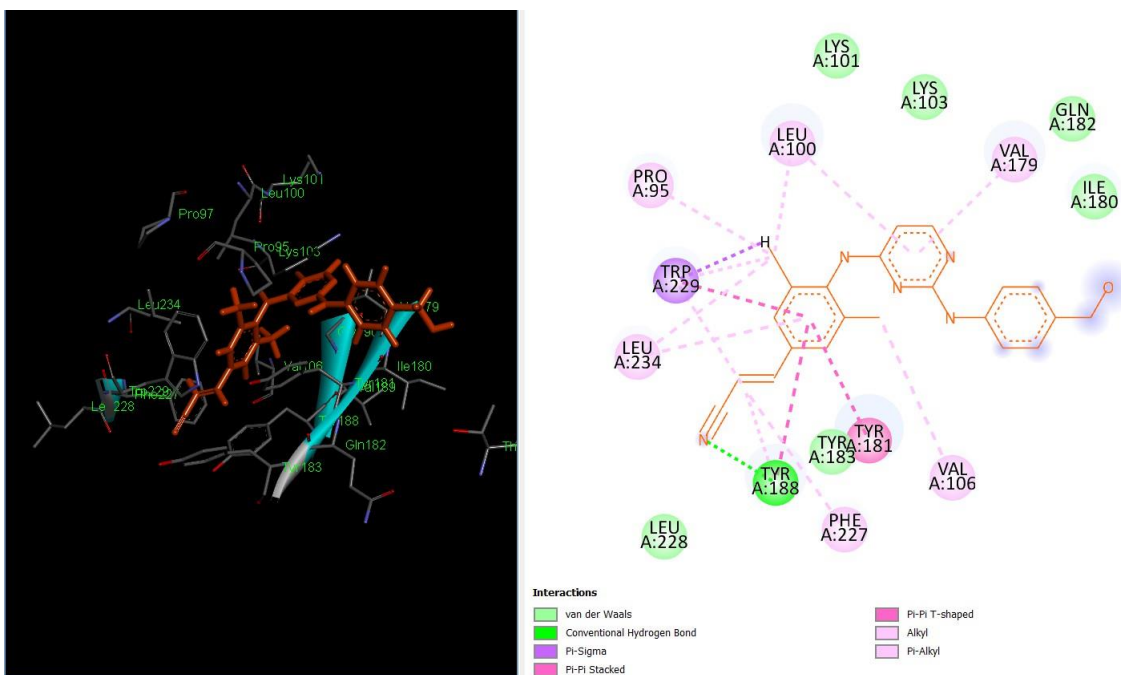
Dockscore of RPV2



RPV2 against 2ZD1 [RT]

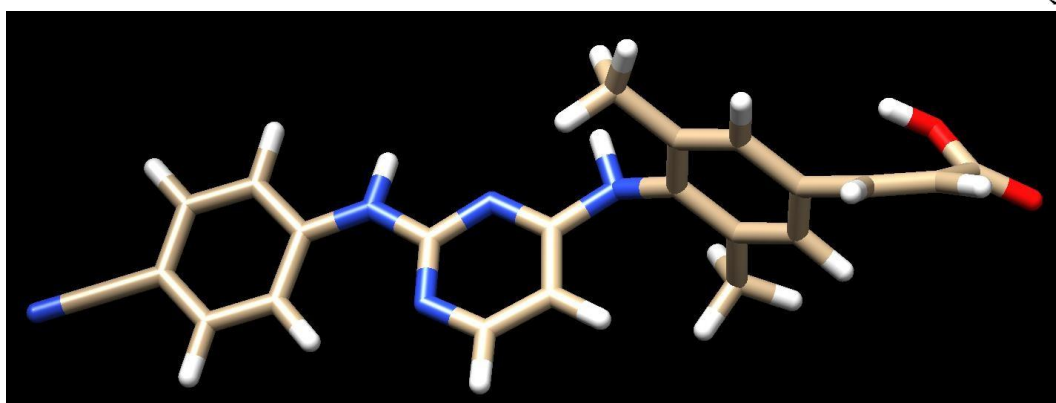
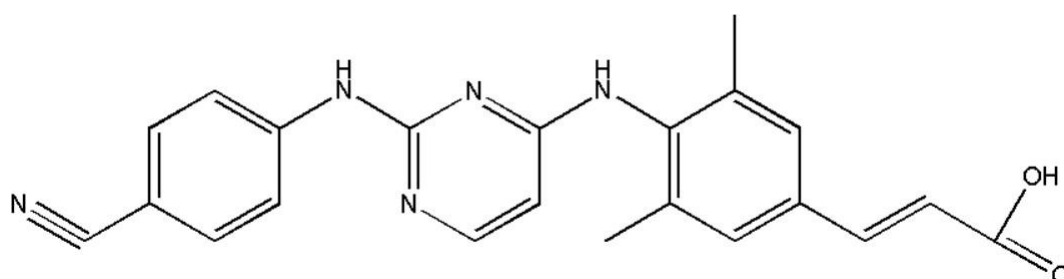


RPV and RPV2



RPV2 2D Interaction

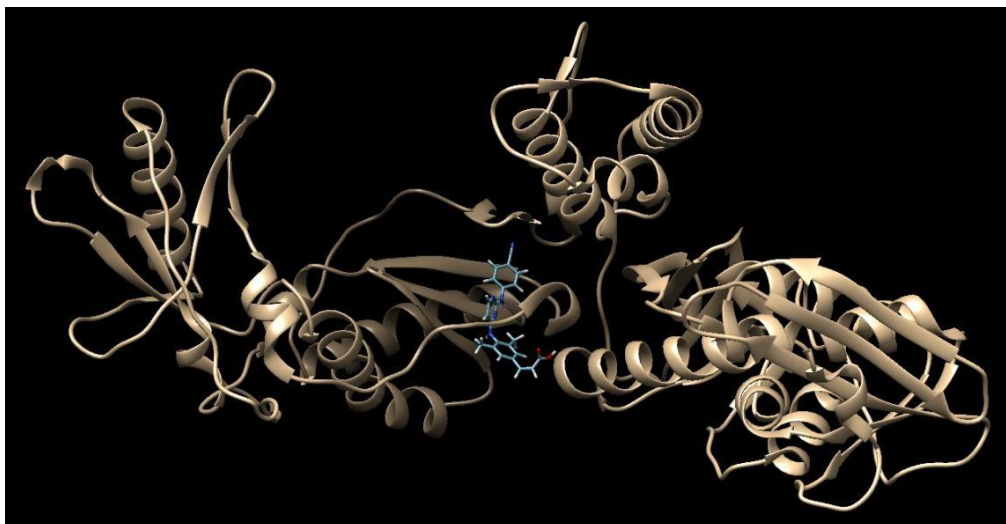
Rilpivirine 3 (RPV3)



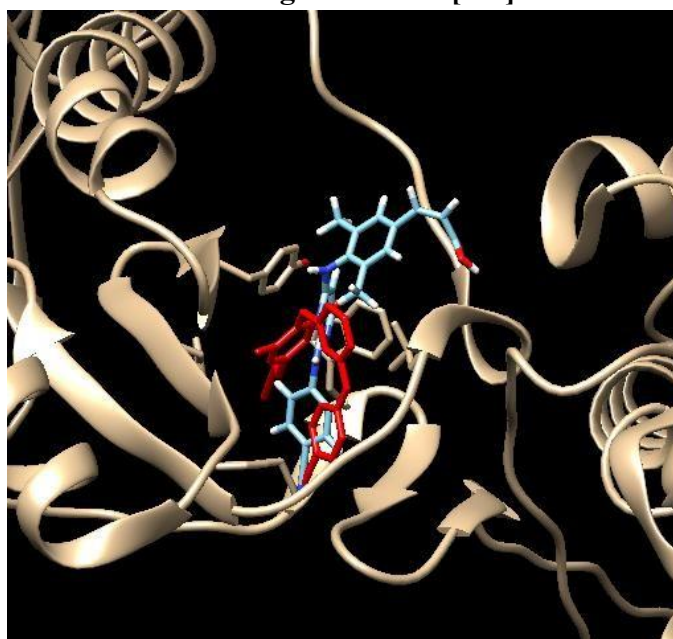
RPV3 3D

S	Score	RMSD l.b.	RMSD u.b.
V	-8.6	0.0	0.0
V	-8.4	3.518	9.521
V	-8.3	4.292	5.156
V	-8.2	4.024	9.821
V	-8.1	3.06	3.989
V	-8.1	3.871	9.646
V	-8.0	2.982	4.254
V	-7.9	4.063	5.016
V	-7.9	2.837	4.291
V	-7.8	1.365	2.507

Dockscore of RPV3



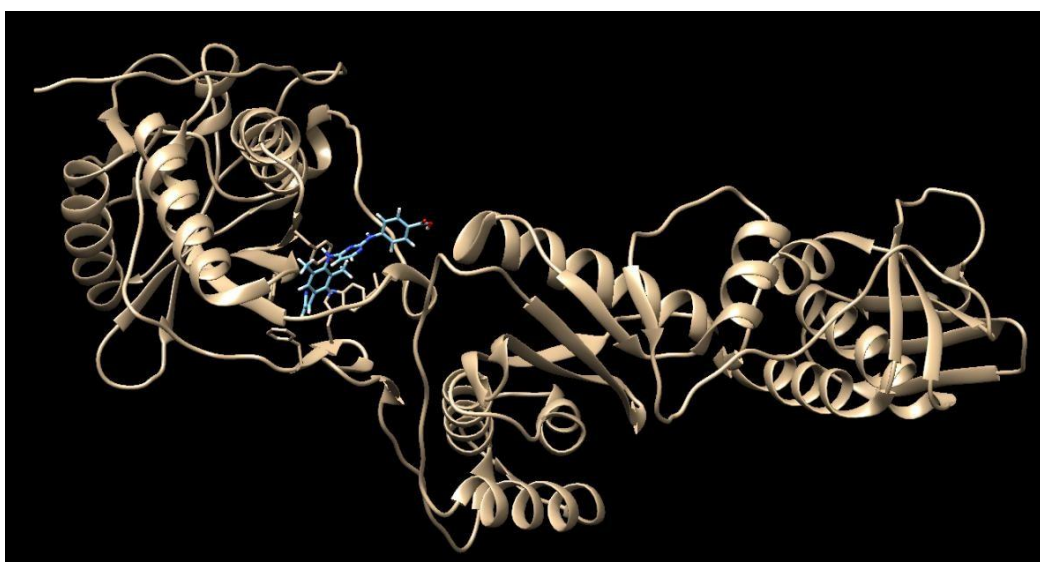
RPV3 against 2ZD1 [RT]



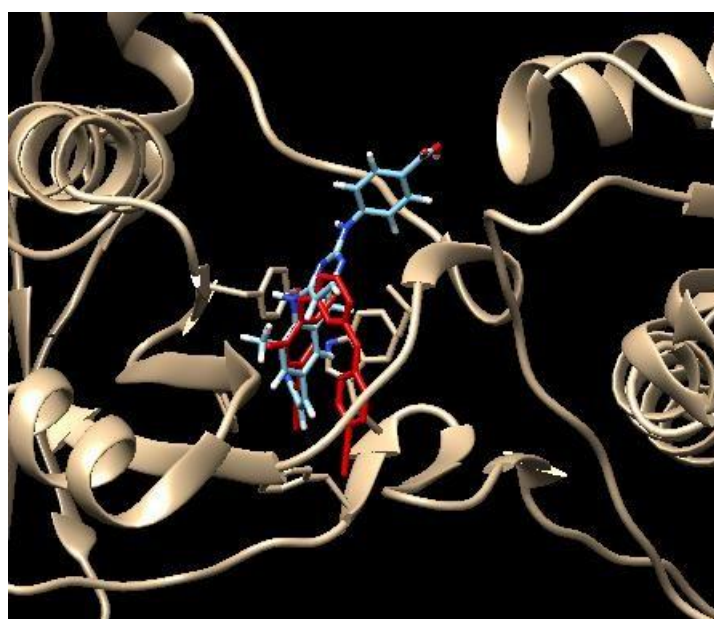
RPV and RPV3

S	Score	RMSD l.b.	RMSD u.b.
V	-8.6	0.0	0.0
V	-8.5	2.949	3.848
V	-8.5	5.148	9.873
V	-8.4	1.979	2.84
V	-8.3	2.663	3.042
V	-8.2	6.041	9.415
V	-8.2	5.446	10.693
V	-8.2	5.225	9.737
V	-8.1	3.235	4.622
V	-7.9	4.992	9.362

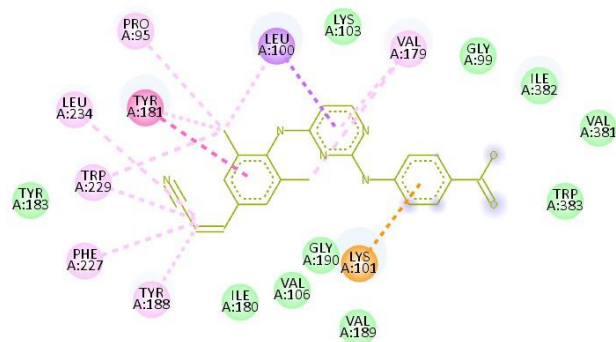
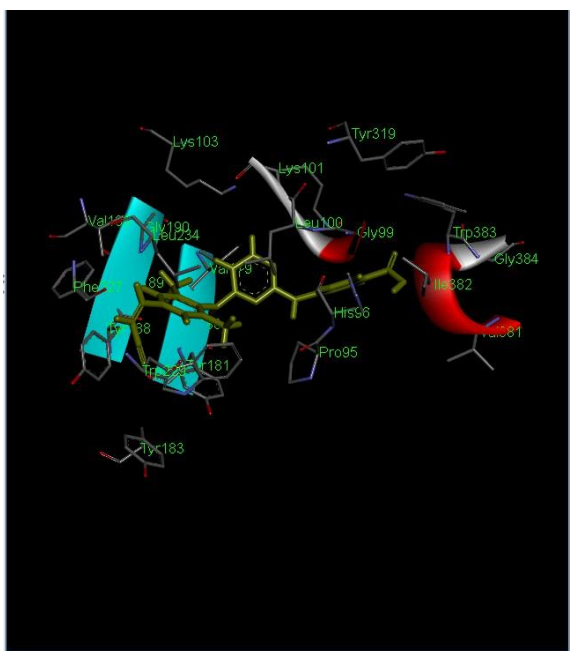
Dockscore of RPV4



RPV4 against 2ZD1 [RT]



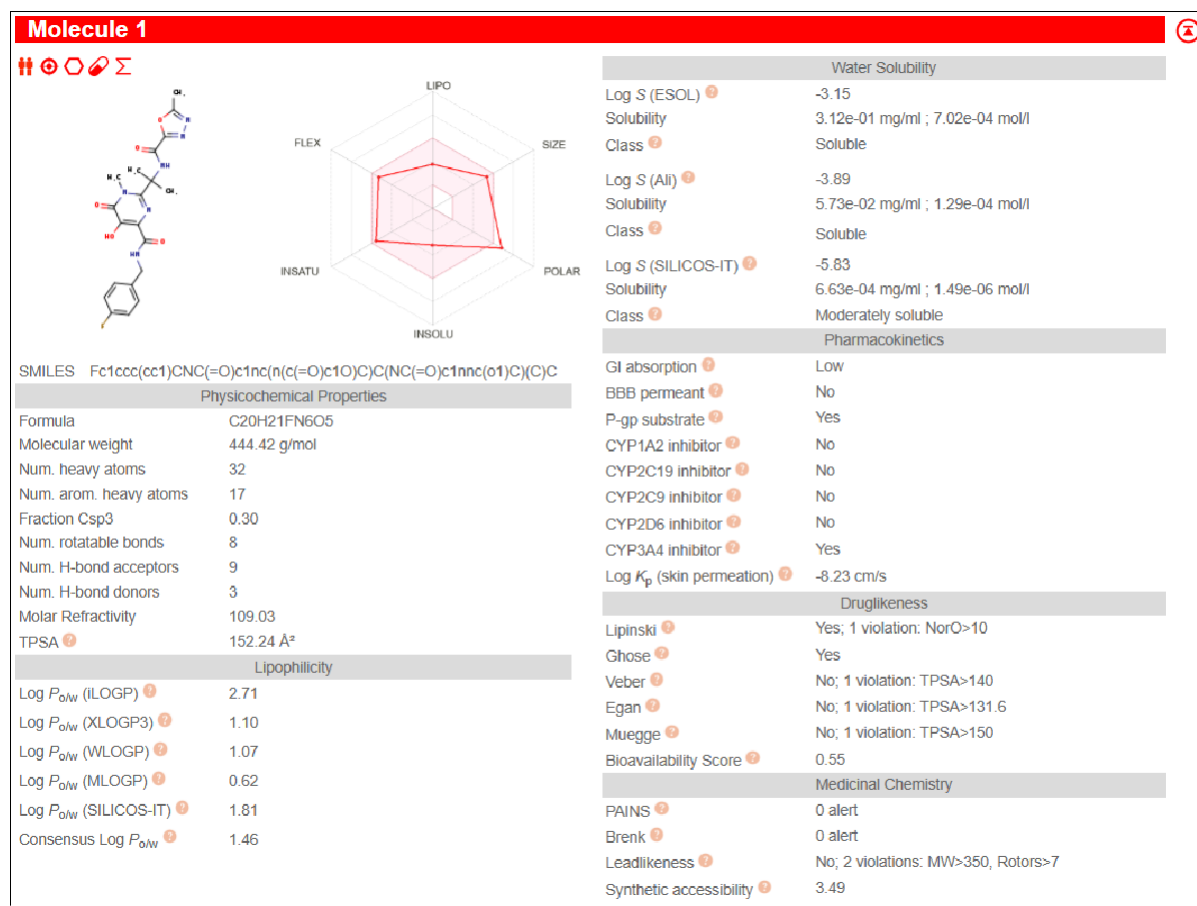
RPV and RPV4



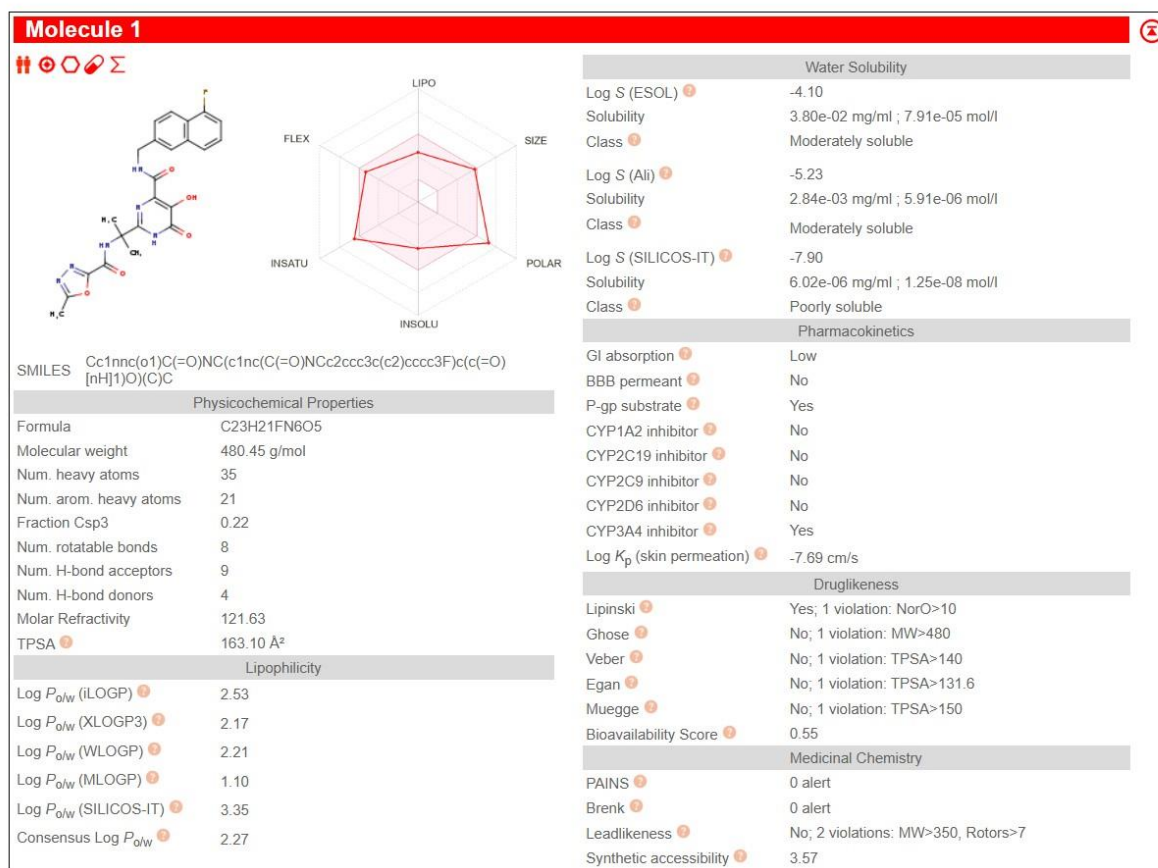
- Interactions**
- van der Waals
 - Pi-Cation
 - Pi-Sigma
 - Pi-Pi Stacked
 - Alkyl
 - Pi-Alkyl

RPV4 2D Interaction

ADME Studies



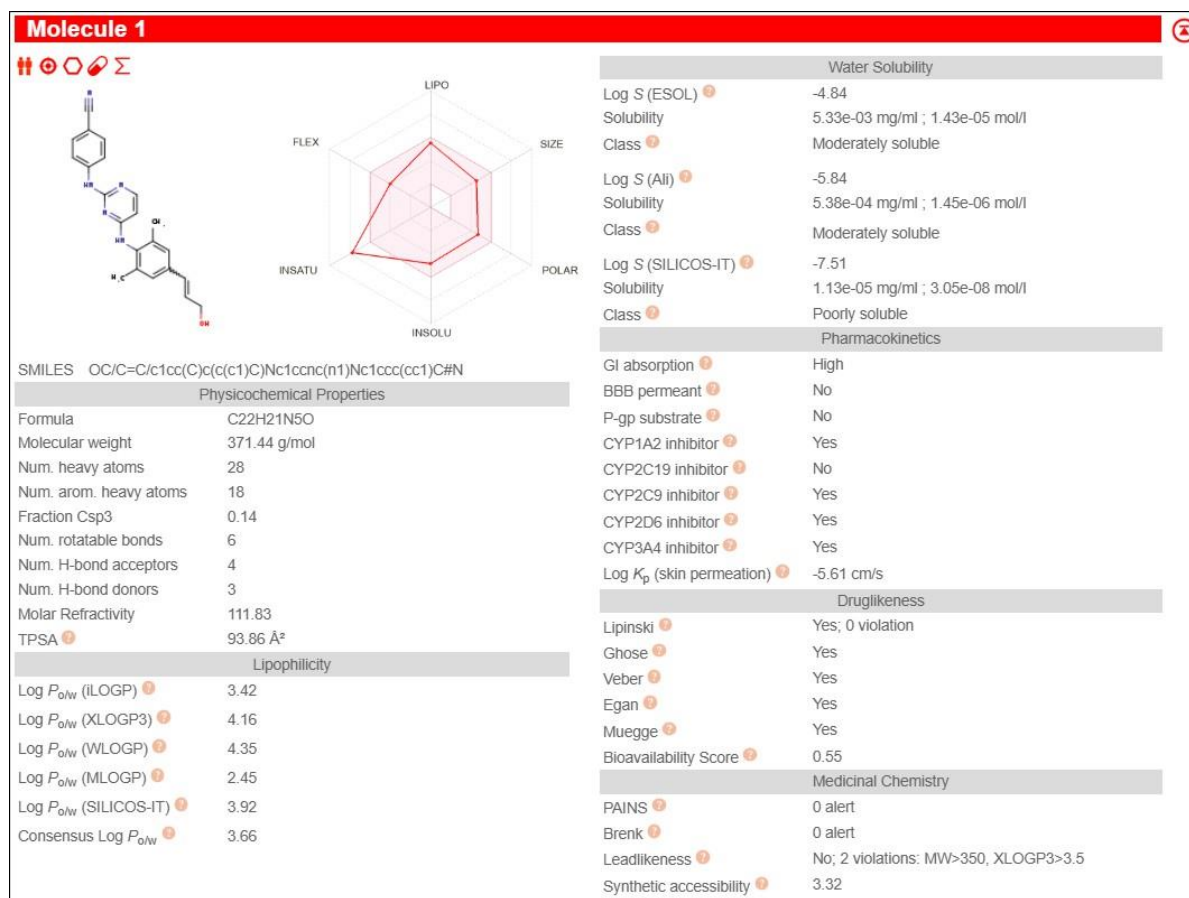
RAL ADME Report



RAL4 ADME Report



RPV ADME Report



RPV1 ADME Report

Results

Parameters of Lipinski Rule of 5

Sr.No.	Parameters	RAL	RAL 4	RPV	RPV 1	Reference value
1	Molecular weight (g/mol)	444.42	480.45	366.42	371.44	Between 160 and 500 Da
2	Log PO/W consensus	1.46	2.27	3.79	3.66	-0.4 and +5.6
3	H donors	3	4	2	3	< 5
	H acceptors	9	9	4	4	< 10

Other Key Findings

Sr.No.	Parameters	RAL	RAL 4	RPV	RPV 1	Reference value
1	TPSA	152.24	163.10	97.42	93.86	90 to 140 Å²
2	Partition coefficient Log K _p (skin)	-8.23	-7.69	-5.30	-5.30	-8 to -11

	permeation)					
3	Bioavailability Score	0.55	0.55	0.55	0.55	≥ 0.55
4	Synthetic assessibility	3.49	3.57	3.29	3.32	≤ 4
5	Molecular refractivity	109.03	121.63	110.41	111.83	40 and 130 cm ³

ADME Interpretation:

The ADME (Absorption, Distribution, Metabolism, and Excretion) report table summarizes key pharmacokinetic properties of four compounds—RAL, RAL 4, RPV, and RPV 1—evaluated against standard reference ranges relevant to Lipinski’s Rule of Five and drug-likeness criteria. All compounds exhibit molecular weights within the acceptable range of 160–500 Da, suggesting favorable size for oral bioavailability. Log P values, indicative of lipophilicity, fall between 1.46 and 3.79, remaining well within the reference threshold of –0.4 to +5.6, which supports balanced hydrophilicity and lipophilicity conducive to membrane permeability. Molecular refractivity, associated with molecular volume and polarizability, is also within the ideal range of 40–130 cm³ for all compounds, pointing to appropriate molecular size and electronic distribution. Additionally, all candidates comply with Lipinski’s criteria for hydrogen bonding, with hydrogen bond donors fewer than 5 and acceptors fewer than 10. Collectively, these findings suggest that all four molecules possess drug-like properties with favorable oral bioavailability profiles.

RAL4 Interaction types and Interaction Residues

Interaction Types	Interaction Residues
Carbon - Hydrogen Bond	TYR (A:129)
Metal Acceptor	Mg (A:396) Mg (A:397)
Pi Ionic	ASP (A:218)
Alkyl/ Pi Alkyl	TYR (A:212)

Interaction types and Residues of RAL4

RPV1 Interaction types and Interaction Residues

Interaction Types	Interaction Residues
Carbon - Hydrogen Bond	TYR (A:188) LEU (A:228)
Pi – Pi Stack / Pi – Pi T Shaped	TYR (A:181) TRP (A:229)
Alkyl/ Pi Alkyl	LEU (A:234) PHE (A:227) VAL (A:106) VAL (A:179)

Interaction types and Residues of RPV

Discussion

The Lipinski Rule of Five (RO5) was used to define the drug-likeness features of Raltegravir (RAL) and Rilpivirine (RPV) derivatives (1-4). Among these, the compounds with the best dockscore and RO5 score were RAL4 and RPV1, respectively. Neither RAL4 nor RPV1 have a log P value greater than 5. Solubility data shows that RPV1 is more soluble than RPV, although RAL4 is less soluble than RAL. Compared to RAL, RPV1 has a lower topological polar surface area (TPSA) score, whereas RAL4 has a higher one. It was found what the ADME characteristics of Raltegravir and Rilpivirine analogues were. This would indicate that the blood-brain barrier was not penetrated. Raltegravir and its analogues had limited GI absorption compared to Rilpivirine and its analogues, which had high GI absorption. In addition, all of the compounds had hydrogen bond donor contributions between two and four bonds, and acceptor contributions between four and nine bonds. Molecular docking studies revealed that RAL 4 and RPV1 have the greatest ability to block the HIV-1 Reverse Transcriptase Enzyme and Integrase enzymes, respectively, when compared to other analogues.

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