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VIRTUAL SCREENING OF NOVEL HIV-RT NNRT INHIBITORS USING ZINC DATABASE

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ABSTRACT: Non-nucleoside reverse transcriptase inhibitors (NNRTI) are a group of small hydrophobic compounds with diverse structure that specifically inhibit HIV-1 reverse transcriptase (RT) by allosteric bind to change its conformation. NNRTIs interact with HIV-1 RT by binding to a single site on the p66 subunit of the p66/p51 heterodimeric enzyme, termed the NNRTI-binding pocket (NNRTI-BP), binding interaction results in both short-range and long-range distortions of RT structure. In this article, we chose T-70(Rilipivirine) as a base structure for virtually identification of more/similar efficient drug like leads then T-70 using five different PDB structures (4KFB, 4IG3, 4IF3, 4GIQ, 3BGR) of RT from PDB database 'RCSB' versus chemical compounds database 'ZINC' using Schrodinger and Discovery Studio software. Using molecular constraint search with similarity coefficient 'Tanimoto', 67500 ligands were extracted and docking analysis resulted in few better efficient in docking properties and in other computational medicinal parameters have reported, and they may further undergo through high end extensive virtual investigation and beyond.

INTRODUCTION: HIV infection is continuing vital issue in way to health concerns, and current studies revels that it remains for a while globally, in the year 2009 over 40 million people were infected worldwide with HIV and the number keeps on growing [1]. Acquired immunodeficiency syndrome (AIDS) is one of the leading causes of death in the world [2]. After rigorous multidisciplinary research worldwide successful development of vaccine is still elusive [3] Importantly when HIV particle infects a host cell its body enzyme reverse transcriptase (RT), an asymmetric 986-amino acids heterodimer) [2] inside its large claw shaped active site, copies the viral single stranded RNA genome into a double-stranded viral DNA.

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The viral DNA is then integrated into the host chromosomal DNA, which then instructs various host cellular processes such as transcription and translation to reproduce the virus. The above mentioned biological processes occurs in HIV virus through the intervention of various enzymes importantly for our research concern pivotal reverse transcriptase (RT), others are protease, integrase etc.

The main functionality of RT is generating the complementary DNA (cDNA) from an RNA template, a process known as reverse transcription. The RT in retrovirus transcribe their single stranded RNA genome into single stranded DNA and to subsequently construct a complementary strand of the first strand of DNA copy, providing a DNA double helix, capable of integration into host cell chromosomes. Functional HIV-RT is a heterodimer containing subunit of 66kDa (p66) and 51kDa (p51), p66 subunit contains two domains, the N terminal polymerase domain(440 residues) and the terminal RNase H domain (120 residues)

p51 is processed by proteolytic cleavage of the polymerase domain of p66 can be described as a "right hand" that contains four subunit((fingers, palm, thumb & connection) [4], the role of the p66 subunits is to carry out the activity of RT whereas it contains the active sites of the enzyme. The p51 is believed to play mainly a structural role [5]. Concern to discover anti retrovirus drug like leads to prohibit better to its biological influence; currently highly active anti retrovirus therapy [6, 7] (HAART, always given as part of combination therapy) includes various classes of RT inhibitors, are using clinically, among that which bind directly to polymerase active site nucleoside inhibitors(NRTIs) and nucleotide RT inhibitors (NtRTIs) or adjacent to it causing an allosteric influence disabling polymerase activity (non-nucleoside RT inhibitors), globally extensive work is under screening by these routes, our work is along the last one. Meanwhile NNRTIs do not bind to the active site of the polymerase but in a less conserved pocket near the active site in the p66 subdomain. Their binding results in a conformational change [4] in the residues that bind DNA that block reverse transcriptase to its enzymatic performance to polymerization and prevent completion of synthesis of the double stranded viral DNA, thus preventing HIV multiplication

MATERIALS AND METHODS:

Rilipivirine: Rilpivirine is an anti-retroviral drug under the umbrella of RT inhibitors (2nd generation), which is used for hindering the activity of the virus (RT). In the work herein Rilpivirine is taken as reference molecule and find out 1% of similar molecules of each retrieved files of zinc drug bank (sd file) using similarity coefficient "Tanimoto" in DS 2.5. In a single job around 1350 molecules was find out as similar as Rilpivirine, we performed as like 50 jobs and a total 50×1350 molecules we found out and perform docking in Schrodinger software.

TABLE 1: DIFFERENT PDBS(RT), LIGAND, CRYSTALLOGRAPHIC PROPERTIES AND MUTATION DETAILS

PDB	Ligand	Resol.	R value	R Free	mutation
4KFB	rilpivirine	1.85	0.186	0.214	C280S
4IG3	rilpivirine	1.95	0.179	0.203	C879S
4IF3	rilpivirine	2.1	0.187	0.213	C879S
4GIQ	rilpivirine	1.51	0.155	0.193	C280S
3BGR	rilpivirine	2.1	0.228	0.269	K103N, K172A, K173A, Y181C, C280S

Reverse transcriptase: X-ray crystal structures of ligand-protein co-complexes have been important tools for medicinal chemists in the discovery, design, and optimization of drug candidates [8, 9, 10]. These structural data, along with the computational analysis tools that have been developed to implement structure-based drug design (SBDD), have proved to be very successful in medicinal chemistry.

As a greater number of X-ray crystal structures become available to medicinal chemists, with the advent of structural genomics [11], computational methods that take advantage of protein-ligand structural data are becoming more critical to the drug design process, in this regard we retrieved following 4KFB, 4GIQ, 4IFY, 4IG3 & 3BGR (see **table 1**) Pbd files from rcsb.org for reverse transcriptase as target having complexed with inhibitor Rilpivirine (T-27) (2nd generation NNRTI, a diarylpyrimide (DAPY) compound, a better bioavailable, soluble and easily formable as medicine then their precursors, approved by the FDA for HIV therapy in May 2011) [12], Crystal structure analysis of HIV-RT enzyme showed that the rilpivirine filled up an allosteric hydrophobic pocket (nonnucleoside binding site, NNBS) and bound the enzyme in a "travelling spaceship- like" (**Fig. 1**) mode.

The lower base of that "spaceship", dimethyl substituted phenyl ring is made of π-electron-rich moiety that interacts through π-π interactions with a hydrophobic pocket formed mainly by the side chains of aromatic amino acids (Tyr-181(A), 188(A), Phe227 (A) and Trp229(A)). On the other hand the upper-half of "spaceship" have a N-phenyl* substituted pyrimidine ring capable of donating and accepting hydrogen bonds with the main chain of the Lys-101(A) (hydrophilic);

Tyr181(A), Tyr188(A), Val-106(A), 179(A),Pro-236(A),Leu-100(A), 234(A) they altogether create a hydrophobic pocket (**Fig. 1a**), rilpivirine in reverse transcriptase (4KFB.pdb) surrounded with amino acids residues are visualized (Glu- 38(B), Lys-101(A), 102(A), 103(A), 238(A), Pro-95(A), 225(A), 226(A), 236(A), Leu-100(A), 228(A), 234(A), Tyr-181(A), 188(A), 318(A), Val-106(A), 179(A), Ile-94(A), 180(A), Asp-237(A), Trp-229(A), Hie-235(A), Glu-138(A), Phe-227(A), Gly-190(A)), during complexation rilpivirine takes a position in NNBS hydrophobic pocket in RT and change its conformation to inhibit the enzymatic activity. Different chemical and structural features make different conformation possibility for the ligands in that pocket which induce desired phenomena. Meanwhile mutation has also considerable impact for drug activity, particularly, the NNRTI resistance reduces due to mutation of Tyr 181(A), and Tyr 188(A) which decreases the π-π interactions; the Gly 190(A) mutation leads to a lower active site space on the front of steric conflict between methyl side chain and the inhibitor, and the formation of a hydrogen bond between K103N(mutant) and Tyr188 reduces the inhibitor entering in the NNBS [13], mutations of some amino acids cause a variation of the NNBS pocket properties, thus decreasing affinities of most the inhibitors.

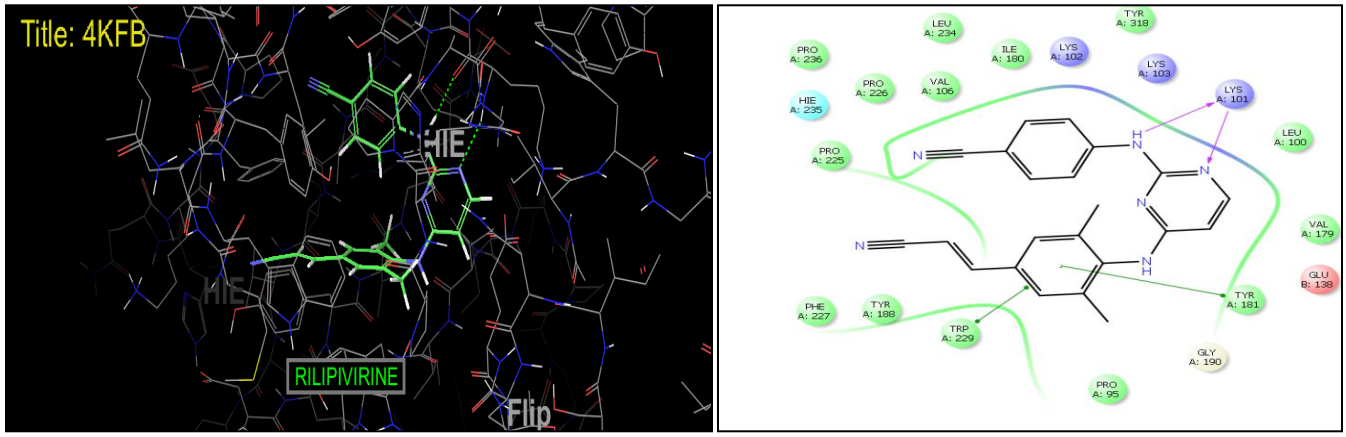

FIG. 1(A): RILIPIVIRINE DOCKED IN PDB KFB, (B) ITS INTERACTION DIAGRAM

In view of the above observations, the design of new NNRTIs require high conformational freedom to accommodate different steric conformations of NNBS and, at the same time, and must contain suitable chemical features capable of interact with highly conserved residues such as Trp229(A) (part of the "primer grip") [14].

EXPERIMENT: 4KFB, 4IG3, 4IF3, 4GI3 & 3BGR all these pdbs are prepared in protein preparation wizard of maestro with following steps- preprocess(default settings), deleting all water molecules and other structures except rilipivirine and generated it states, optimization , and minimization(with OPLS2005 forcefield) and saved all in pre created directory folder corresponding Grids are generated in these prepared pdbs with the centre defined by the co-crystalized ligand T-27(Rilipivirine) with default settings, ligands as similar to rilpivirine with DS V2.5 in job " find similar molecules" with settings 1% similar molecules identification as similar to rilipivirine and similarity coefficient 'tanimoto' which is very well known accurate similarity measures, remaining are default. Similar ligands are prepared for docking jobs in 'ligprep' with deselected options 'desalt' and 'generate tautomers' and generate low ring conformations 100 per ligands using 'epik' and docked in corresponding grids of pdbs.

All docking calculations are performed using the "Extra Precision"(XP) mode of Glide Program with default settings including various rewards calculations, partial charge of ligands and similarity to T-27, all jobs were done on Intel i-7 3770K (unlocked) quad core machine with bios setting 4.5 GHz with GSkill 8GB RAM & Corsair H-70 liquid cooling system. Medicinal parameters were calculated using qikprop **(Tables 2-6)**

TABLE 2: PDB-4KFB) DOCKING SCORE AND OTHER CALCULATED PROPERTIES DETAILS

Title	D.S.	ip	rtvFG	CNS	dipole	SASA	QPlogHERG	QPlogBB	QPPMDCK	QPlogKp	metab	QPlogKhsa	PHOAbs
ZINC52690626	-15.6	-7.1	0	0	3.487	637	-5.893	-0.592	975.199	-1.36	4	0.607	100
ZINC70032478	-15.5	-7.4	1	-2	8.018	664	-5.536	-1.917	54.109	-3.431	4	0.033	78.872
T-27	-15.47	-7.8	0	-2	12.8	651	-5.613	-1.746	64.973	-3.233	4	0.329	84.403
ZINC70032481	-15.37	-7	1	-2	7.664	643	-5.088	-1.873	44.082	-3.592	4	0.064	77.254
ZINC70032479	-15.29	-7	1	-2	8.68	672	-5.619	-2.012	44.999	-3.559	4	0.064	77.736
ZINC49393660	-15.22	-7.2	1	-2	8.023	671	-5.97	-1.964	50.98	-3.212	5	0.055	79.216
ZINC70032480	-15.19	-7.1	1	-2	7.04	725	-6.584	-2.121	55.367	-3.144	4	0.155	81.725
ZINC49392314	-15.08	7.1	1	-2	4.449	595	-5.034	-1.562	78.874	-2.902	5	-0.121	79.956
ZINC15880588	-15.06	-7	0	-1	10.46	618	-3.907	-0.402	1446.922	-1.568	6	-0.001	100
ZINC05298157	-15.06	-7	0	-2	3.932	661	-5.312	-1.054	372.006	-2.158	5	0.378	100
ZINC69934799	-15.05	-7	1	-2	5.486	694	-6.41	-2.158	42.782	-3.3	5	0.053	77.927
ZINC49391897	-15.03	-7	0	-2	5.679	620	-5.445	-1.872	39.644	-3.803	4	-0.102	72.895
ZINC49391715	-15.03	-7	0	-2	5.206	640	-5.764	-2.033	37.517	-3.702	3	-0.109	73.178

(D.S. (Docking Score, kcal/mol), Lip(Lipophilicity), rtvFG(no. of reactive functional groups, 0 – 2), CNS(Predicted central nervous system activity on a –2 (inactive) to +2 (active) scale),Dipole(computed dipole moment, 1.0 – 12.5), SASA(Total solvent accessible surface area (SASA) in square angstroms using a probe with a 1.4 Å radius, RANGE- 300.0 – 1000.0), QPlogHERG (Predicted IC50 value for blockage of HERG K+ channels, concern below –5), QPlogBB(Predicted brain/blood partition coefficient, –3.0 – 1.2), QPPMDCK(Predicted apparent MDCK cell permeability in nm/sec, <25 poor, >500 great), QPlogKp (Predicted skin permeability, log *K*p, –8.0 – –1.0), metab (Number of likely metabolic reactions, 1 – 8), QPlogKhsa(Prediction of binding to human serum albumin, –1.5 – 1.5), PHOAbs(Predicted human oral absorption on 0 to 100% scale, >80% is high, <25%ispoor)

TABLE:-3(4IG3)

Title	D.S.	Lip	#rtvFG	CNS	dipole	SASA	QPlogHERG	QPlogBB	QPPMDCK	QPlogKp	metab	QPlogKhsa	PHOAbs
ZINC52690626	-15.58	-6.85	0	0	5.983	635.955	-5.733	-0.556	1250.514	-1.515	5	0.604	100
RILIPIVIRINE	-15.23	-8.06	0	-2	12.969	665.355	-5.937	-1.818	65.436	-3.185	4	0.325	84.554
ZINC70032481	-14.51	-6.95	1	-2	7.321	685.288	-5.961	-1.969	56.415	-3.256	4	0.084	80.38
ZINC70032478	-15.22	-7.14	1	-2	8.23	694.959	-5.771	-2.127	38.532	-3.682	4	0.155	77.755
ZINC49393660	-14.77	-7.35	1	-2	7.7	630.735	-5.284	-1.787	55.509	-3.274	5	-0.02	78.354
ZINC70032479	-14.47	-6.95	1	-2	8.885	654.71	-5.34	-1.858	51.333	-3.406	4	0.085	79.127
ZINC70032480	-14.75	-7.32	1	-2	9.255	670.938	-5.677	-2.046	42.59	-3.584	4	0.044	77.011
ZINC05298157	-14.67	-7.86	0	-2	2.414	684.199	-5.742	-1.136	352.19	-2.127	5	0.41	100
ZINC49391715	-14.89	-6.85	0	-2	5.592	625.381	-5.634	-1.981	37.511	-3.675	3	-0.14	72.673
ZINC49392621	-14.73	-6.64	1	-2	5.78	615.791	-5.703	-1.913	55.195	-3.398	2	-0.178	73.632
ZINC49392310	-15.1	-7.2	1	-2	5.008	653.115	-5.93	-1.795	67.835	-2.886	5	0.004	81.12

TABLE:-4(4IF3)

Title	D.S.	Lip	rtvFG	CNS	dipole	SASA	QPlogHERG	QPlogBB	QPPMDCK	QPlogKp	metab	QPlogKhsa	PHOAbs
RILIPIVIRINE	-15.6	-8.02	0	-2	12.957	667.793	-5.977	-1.832	64.629	-3.189	4	0.329	84.508
ZINC70032481	-15.33	-7.44	1	-2	7.811	638.234	-5.032	-1.85	45.603	-3.578	4	0.049	77.29
ZINC70032479	-15.28	-7.51	1	-2	9.507	659.814	-5.417	-1.911	49.619	-3.479	4	0.064	78.513
ZINC70032480	-15.21	-7.2	1	-2	6.989	721.087	-6.538	-2.118	54.303	-3.167	4	0.145	81.367
ZINC52690626	-15.68	-7.22	0	0	3.411	638.004	-5.911	-0.611	921.618	-1.379	4	0.606	100
ZINC70032478	-15.48	-7.44	1	-2	7.755	662.455	-5.523	-1.838	64.246	-3.283	4	0.037	80.471

TABLE:-5(4GIQ)

Title	D.S.	Lip	#rtvFG	CNS	dipole	SASA	QPlogHERG	QPlogBB	QPPMDCK	QPlogKp	metab	QPlogKhsa	PHOAbs
T-70	-15.71	-7.95	0	-2	12.715	669.04	-5.97	-1.839	63.147	-3.204	4	0.342	84.456
ZINC70032481	-15.24	-7.34	1	-2	7.825	640.43	-5.119	-1.894	44.135	-3.626	4	0.02	76.592
ZINC70032480	-15.22	-7.32	1	-2	8.864	670.93	-5.662	-2.01	45.633	-3.526	4	0.052	77.746
ZINC70032478	-15.19	-7.48	1	-2	7.735	668.59	-5.6	-1.898	58.15	-3.354	4	0.052	79.848
ZINC15880588	-15.1	-7.42	0	-1	10.571	629.23	-4.177	-0.414	1480.1	-1.485	6	0.012	100
ZINC05298157	-15.06	-7.84	0	-2	3.676	675.11	-5.579	-1.071	384.76	-2.067	5	0.408	100
ZINC70032479	-14.99	-7.32	1	-2	9.456	657.72	-5.381	-1.907	49.287	-3.493	4	0.06	78.359
ZINC52690626	-14.83	-6.62	0	0	6.065	629.36	-5.631	-0.522	1326.263	-1.486	4	0.59	100

TABLE:-6(3BGR)

Title	DS	XP PhobEn	XP L'philic	rtvFG	CNS	SASA	QPlogHERG	QPlogBB	QPPMDCK	QPlogKp	#metab	QPlogKhsa	PHOAbs
ZINC70032481	-16.3	-2.7	-7.4	1	-2	649	-5.241	-1.848	54.174	-3.469	4	0.029	78.615
ZINC70032478	-16.2	-2.7	-7.39	1	-2	636	-5.041	-1.885	41.066	-3.64	4	0.04	76.249
ZINC70032479	-16.1	-2.7	-7.31	1	-2	661	-5.432	-1.955	45.843	-3.56	4	0.057	77.69
ZINC05298157	-15.7	-2.7	-7.61	0	-2	666	-5.407	-1.054	379.018	-2.109	5	0.394	100
ZINC70032480	-15.7	-2.7	-6.92	1	-2	672	-5.759	-1.915	58.237	-3.281	4	0.048	79.984
ZINC69934802	-15.6	-2.7	-7.07	1	-2	628	-5.451	-1.939	41.812	-3.483	5	-0.09	74.901
ZINC49391769	-15.6	-2.7	-6.67	1	-2	604	-5.169	-1.706	94.682	-3.519	2	-0.136	74.929
ZINC49393660	-15.6	-2.68	-6.91	1	-2	618	-5.203	-1.818	51.32	-3.397	5	-0.106	76.267
ZINC49392321	-15.6	-2.69	-6.92	1	-2	612	-5.48	-1.829	48.765	-3.21	5	-0.133	75.837
ZINC49391715	-15.6	-2.68	-6.62	0	-2	635	-5.709	-2.029	36.98	-3.73	3	-0.129	72.694
RILIPIVIRINE	-15.6	-2.22	-7.6	0	-2	663	-5.838	-1.776	68.042	-3.161	4	0.345	85.073
ZINC49392621	-15.6	-2.7	-6.41	1	-2	626	-6.011	-2.003	43.213	-3.267	2	-0.169	73.861
ZINC49392314	-15.6	-2.7	-6.95	1	-2	615	-5.44	-1.941	36.012	-3.463	5	-0.106	73.491
ZINC49391718	-15.6	-2.7	-6.5	0	-2	627	-5.51	-1.983	36.85	-3.767	3	-0.124	72.581
ZINC49393663	-15.5	-2.7	-6.98	1	-2	623	-5.373	-1.866	47.52	-3.381	5	-0.098	75.89
ZINC69934799	-15.5	-2.7	-6.87	1	-2	709	-6.686	-2.284	36.812	-3.338	5	0.081	77.235
ZINC49392310	-15.5	-2.7	-6.85	1	-2	629	-5.794	-1.937	43.002	-3.233	5	-0.101	75.453
ZINC05298148	-15.4	-2.7	-6.9	0	-2	653	-5.741	-1.695	48.239	-3.681	3	0.117	76.771

RESULT AND DISCUSSION: In our virtual investigation we find following 'ZINC' molecules close similar in docking score in comparison to T-27 , in different pdbs (see Table 2) (4KFB), 3(4IG3), 4(4IF3), 5(4GIQ)& 6(3BGR) but through our investigation a no of screened molecules are failed in its various medicinal properties, ZINC52690626, ZINC70032478 both having marginally better docking score then T-27 the interaction for later one is noticeable **(Fig. 2, 3))** due to π-π interaction between the ethyl substituted phenyl ring with TRP-229(A) and one additional H-bond between amino substituted triazine with the GLU-138(B) both interactions are in considerable strength which may make some different, lipophilic nature (Lip) is also close similar to T-27, rtvFG (reactive functional group) better for ZINC52690626, QPPMDCK (Predicted apparent MDCK cell permeability (in nm)) value is more noticeable for ZINC52690626 which is very much better then T-70, the PHOAbs(Predicted human oral absorption) is also 100%. In Table-3, (4IG3) ZINC52690626 again showing much better QPPMDCK properties with good increment.

In **Table 4,** (4IF3) shows the same trend as previous, but in **Table-5**(4GIQ) we see that the docking score change marginally for ZINC52690626 and in Table-6(3BGR) ZINC70032481(-16.37), ZINC70032478(16.21), ZINC49391715(-15.65) ZINC70032479(-16.1), ZINC05298157(-15.75) & ZINC49391718(-15.57) show better docking score, ZINC70032481, ZINC70032478 & ZINC49391715 all these have three reactive functional groups as the computed data showing which may be some drawback for such molecules since rilpivirine shows no any reactive functional group, but ZINC05298157, ZINC49391715 & ZINC49391718 are nearly to T-27 in docking scores and these showing no any reactive functional group, so these may be an advantage, we see that all molecules (in Table 6 (3BGR)) are showing CNS(Predicted central nervous system activity) negative, lipophilicity in between (-7.89 to -6.43), rilpivirine is in top but these ZINC molecules are also close to it, since lipophilicity has very important impact on drug design procedure.

ZINC70032481 **(Fig. 3.)** interact with following amino acids LYS-101(A) with both donar and acceptor H-bonding and another H-bond donar by substituted amino group on triazine ring to GLU-138(B), π-π interaction between ethyl substituted benzene ring of the ligand to TRP-229(A) these four major interaction increased significantly D.S. compare to T-27, computed CNS activity is normal, calculated properties in desired range the interaction are considerable in strength additionally its other calculated properties are also in desired limits, its PHOAbs (Predicted qualitative human oral absorption) is 100% and QPPMDCK(Predicted apparent MDCK cell permeability) is also much better then T-70 and dipole moment is in range.

The 3BGR have five mutations (K103N, K172A, K173A, Y181C & C280S) in this regard the increment in docking result is very well and noticeable and it may be more effective towards such mutants, which is more advantageous in this regard.

In 4KFB **(Fig 2.),** ZINC70032478(-15.5) interacts with LYS-101(A) (both hydrogen bond donar with secondary amino group and H-bond acceptor by triazine nitrogen,TRP-229(A) interact with π-π interaction with substituted phenyl ring and GLU-138(B) acts as H-bond acceptor . ZINC70032481(-15.37) also interacts with corresponding same amino acids, both are diastereomeric to each other, this outcome is very important to synthesis point of view, protonated ZINC52690626(-15.6) is showing some better docking score and showing interactions with LYS-101(A) both donar and acceptor for H-Bonding and π-π interaction with LYS-103(A) and TYR-181(A), its protonation is activated by α-dimethylamino substitution on pyridine ring, which may prone to get protonated at stomach pH range and if it will happen, become an advantage, protonated pyridine ring interact by H-bonding with TRP-229(A), all above three have lipophilicity between -7.1 to 7.0 which is almost near to T-27(-7.8) QPPMDCK (Predicted apparent MDCK cell permeability in nm/sec, <25 poor, >500 great) is noticeable for ZINC52690626 is 975.2 which is very well and PHOAbs is also 100% which QPlogKhsa (Prediction of binding to human serum albumin, –1.5 – 1.5) value is 0.607, for rilpivirine its 0.329 so better complexion to albumin, QPlogKp(Predicted skin permeability, log *K*p, –8.0 – –1.0) is -1.36 which is more than two time to rilpivirine rtvFG(no. of reactive functional groups) is none but showing some CNS activity, ZINC15880588 have very high QPPMDCK value, QPlogKhsa values is very low but PHOAbs value is 100%, ZINC05298157 also showing 100% PHOAbs value. So herein both less mutant and more mutant showing some noticeable computationally calculated properties.

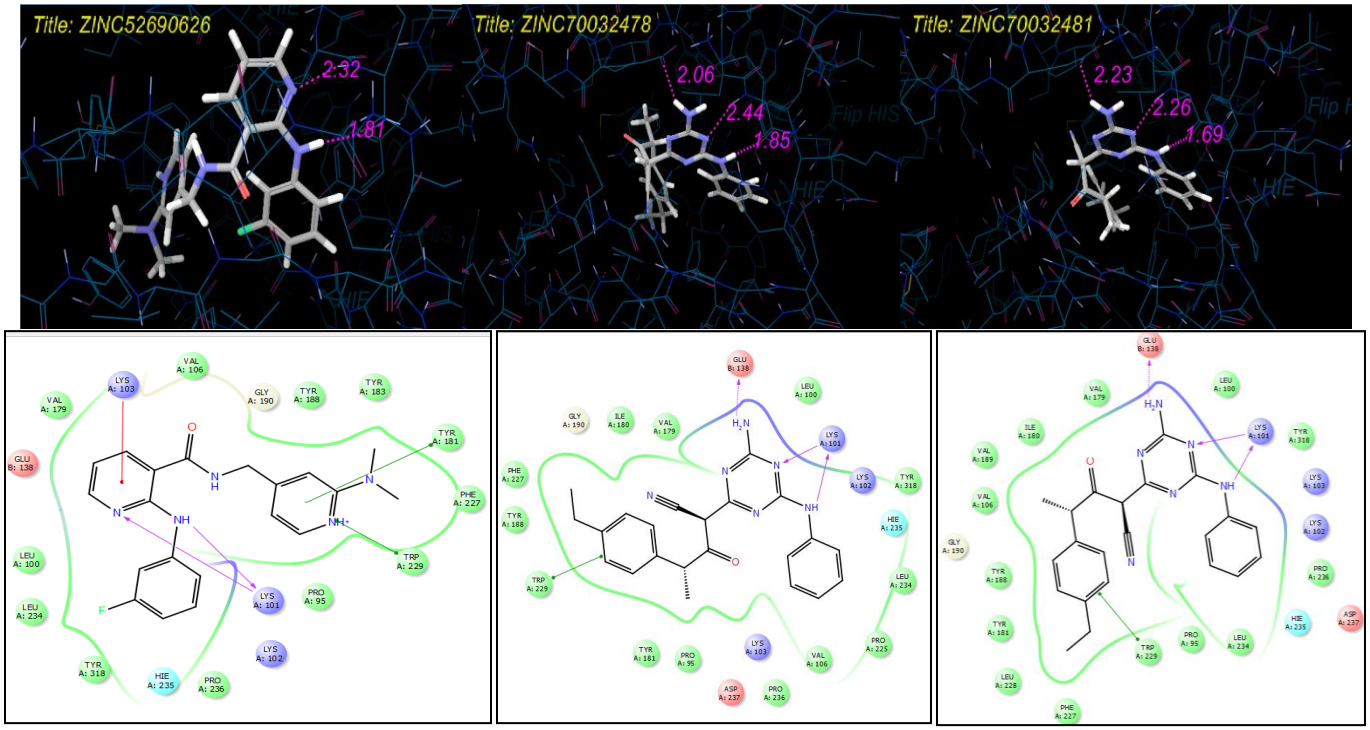

FIG. 2: 4KFB (RT) WITH DOCKED LIGAND ZINC52690626, 70032478 & 70032481 AND CORRESPONDING INTERACTION DIAGRAMS (BELOW)

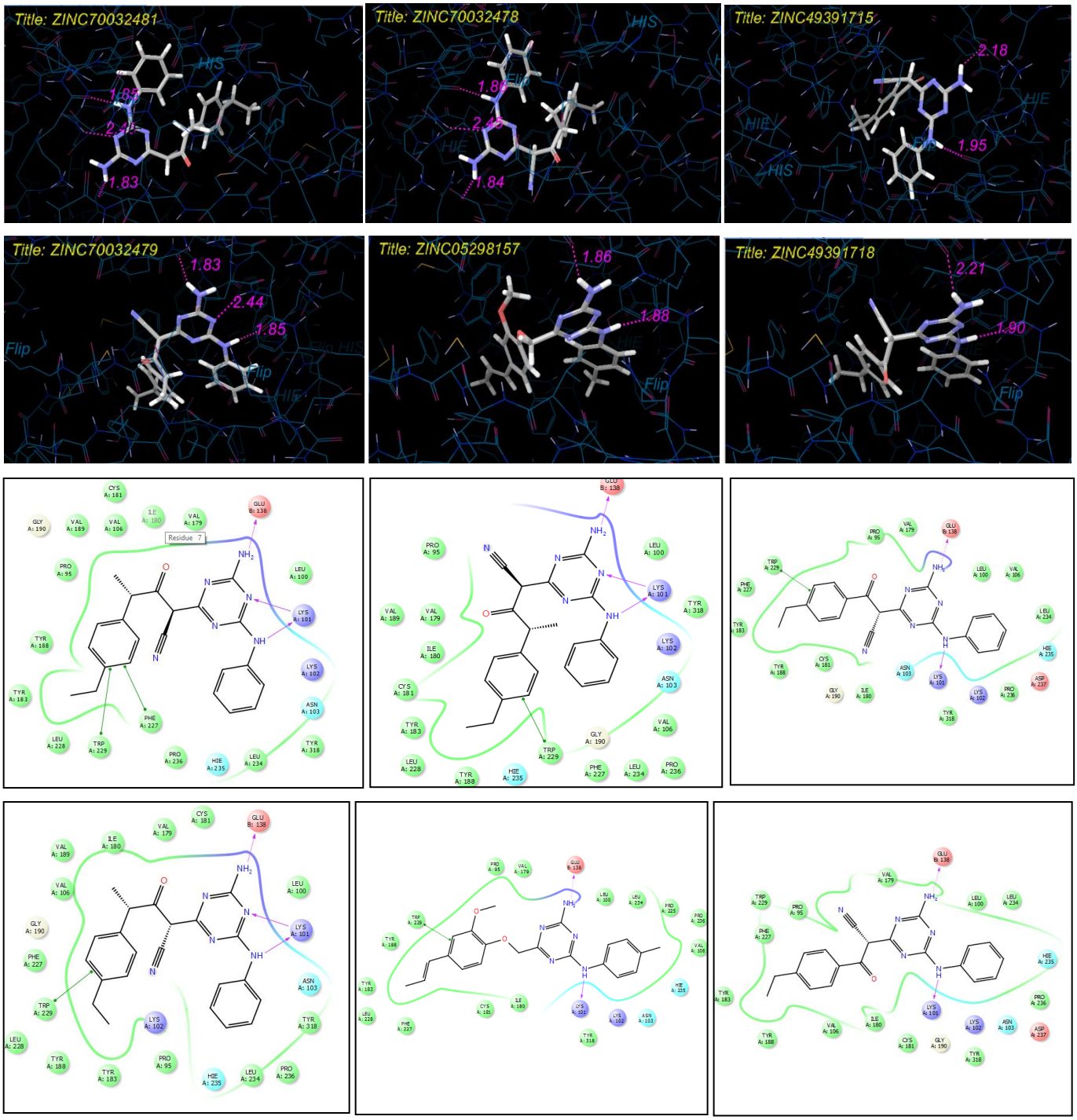

FIG. 3: (A) 3BGR (RT) WITH DOCKED LIGANDS ZINC70032481, ZINC70032478, ZINC49391715, ZINC70032479 ZINC05298157 & ZINC49391718, CORRESPONDING INTERACTION PATTERN IN (B)

CONCLUSION: In this work, we have tried to recognized some more/similar potent drug like leads instead 'Rilipiviine (T-70)' which may be more effective, we used five different RT crystallographic structures for better identification/verification for our results, ZINC70032481, ZINC70032478, ZINC70032479, ZINC05298157 & ZINC52690626 are showing very fine computed properties therefore, this study verify the importance of small drug like molecules libraries as like 'ZINC. Docking.org' and their use certainly help scientific groups to enhance their capabilities in drug discovery with reducing time, including drug discovery process prior synthesis. Herein identified molecules may further investigate instead "*in silico*".

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