Electronic Supplementary Material (ESI) for RSC Advances.

Delving into Zika Virus Structural Dynamics- A Closer look at NS3 Helicase Loop flexibility and its Role in Drug Discovery

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Supplementary Data

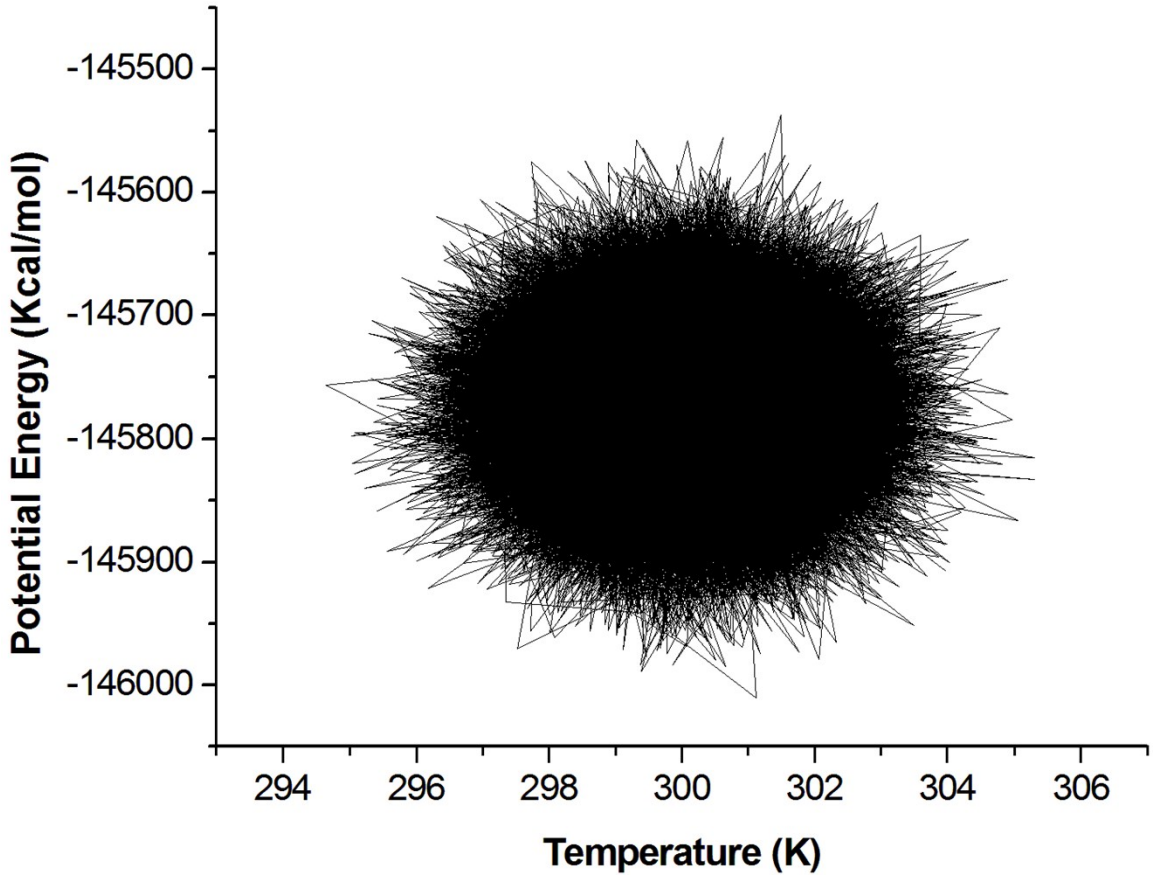

Figure S1: Potential Energy Fluctuations of the NITD008-NS3 Helicase System at varying temperatures during the 100ns simulation. The average temperature of the system was 300K and the average potential energy was -145774 kcal/mol.

Energy Components (kcal/mol)					
	Δ E_{vdW}	**ΔE_{elec}**	**ΔG_{gas}**	**ΔG_{solv}**	**ΔG_{bind}**
ZIKV NS3 Helicase	-3573.27 ± 30.81	-30020.42 ± 127.46	-33593.70 ± 140.40	-4481.84 ± 97.48	-38075.53 ± 73.37
NITD008 (Pose 1)	-4.82 ± 1.08	-12.26 ± 5.98	7.43 ± 6.09	-24.39 ± 1.89	-16.96 ± 5.29
Complex	-32.11 ± 4.09	-31.36 ± 8.72	-63.46 ± 9.18	33.47 ± 4.56	**-30.00 ± 5.58**

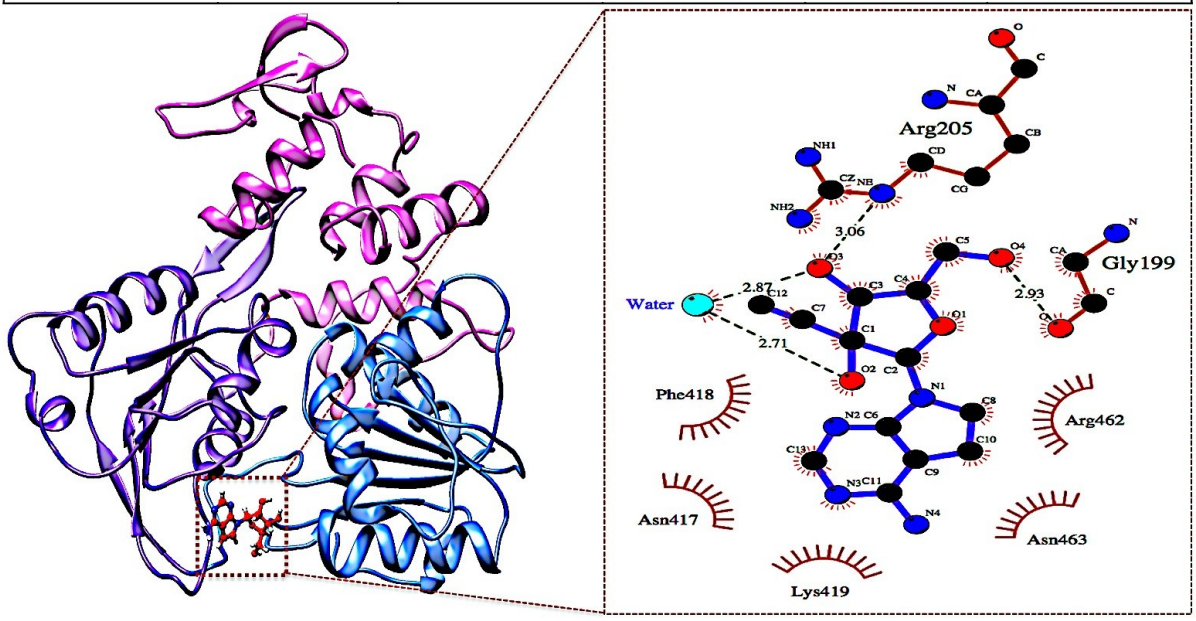

Figure S2: Complex of NITD008-NS3 Helicase with a Docking score of -7.7 kcal/mol. MM/GBSA calculations yielded a result of -30.00 kcal/mol. The ligand shifted further out of the hydrophobic pocket after 150ns of the simulation. This may possibly be due to the ligand not interacting with the stabilizing residues of the P-loop.

Energy Components (kcal/mol)					
	Δ E_{vdW}	**ΔE_{elec}**	**ΔG_{gas}**	**ΔG_{solv}**	**ΔG_{bind}**
ZIKV NS3 Helicase	-3567.30 ± 31.08	- 29710.32 ± 175.80	-33277.62 ± 178.68	-4790.36 ± 137.78	-38067.98 ± 76.12
NITD008 (Pose 2)	-5.47 ± 1.01	-6.34 ± 7.85	0.87 ± 7.35	-27.84 ± 3.89	-26.97 ± 5.17
Complex	-24.12 ± 2.75	-9.35 ± 7.29	-33.47 ± 6.78	19.80 ± 5.62	**-13.67 ± 3.01**

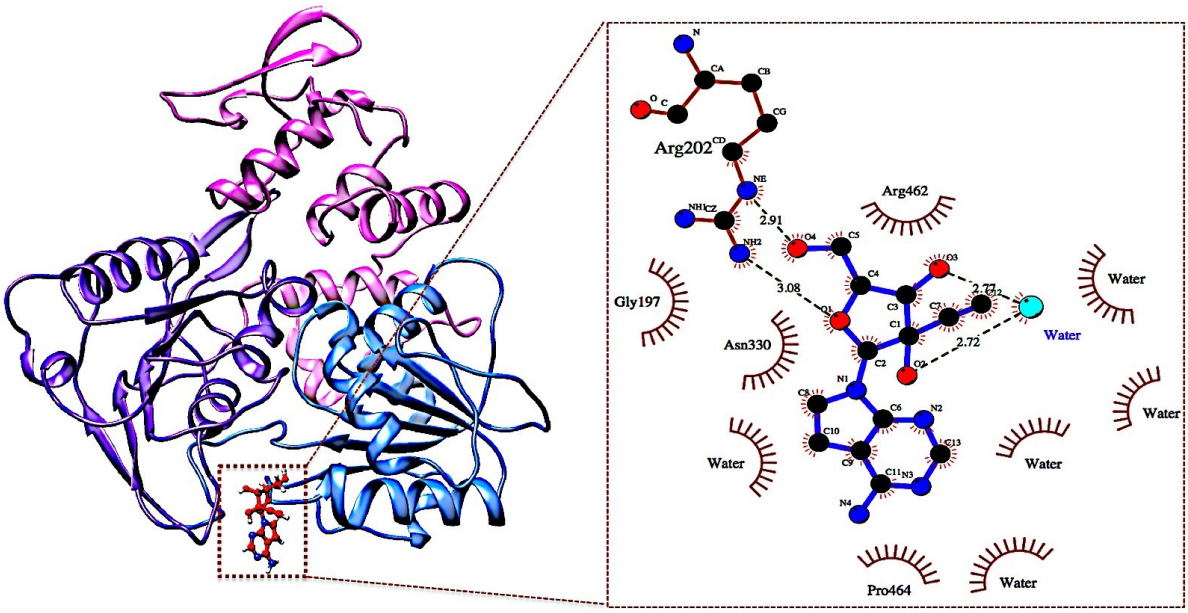

Figure S3: Complex of NITD008-NS3 Helicase with a Docking score of -7.6 kcal/mol. MM/GBSA calculations yielded a result of -13.67 kcal/mol. The ligand docked out of the hydrophobic pocket and during the simulation, due to the lack of stabilizing interactions, the ligand moved further out of the active site and into the solvent.

Energy Components (kcal/mol)					
	Δ E_{vdW}	**ΔE_{elec}**	**ΔG_{gas}**	**ΔG_{solv}**	**ΔG_{bind}**
ZIKV NS3 Helicase	-3564.79 ± 26.89	- 29878.89 ± 131.37	-33443.68 ± 133.78	-4633.21 ± 88.03	-38076.89 ± 68.96
NITD008 (Pose 3)	-5.56 ± 0.60	10.53 ± 6.58	4.96 ± 6.51	-28.45 ± 3.51	-23.49 ± 4.78
Complex	-17.75 ± 4.65	-14.45 ± 7.46	-32.21 ± 8.76	20.35 ± 5.95	**-11.86 ± 6.37**

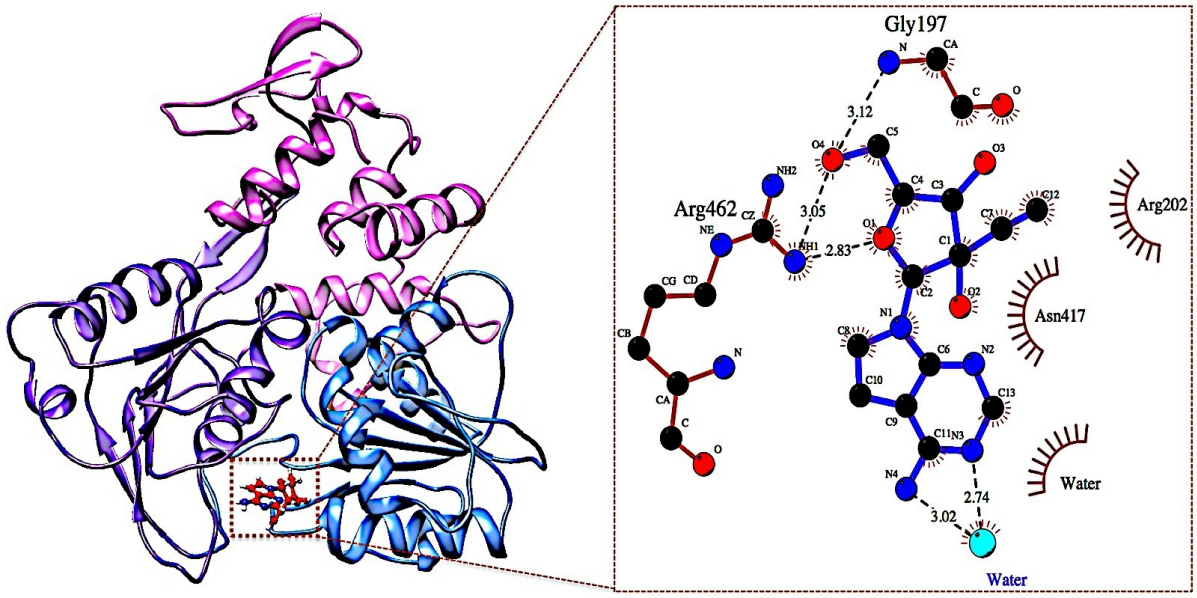

Figure S4: Complex of NITD008-NS3 Helicase with a Docking score of -7.1 kcal/mol. MM/GBSA calculations yielded a result of -11.86 kcal/mol. This ligand showed a similar pose to that of the -7.6 kcal/mol-docked pose, however, there was only one residue, Arg462, which showed stabilizing hydrogen bonds with the terminal oxygen located on the ribose group of NITD008.

Energy Components (kcal/mol)					
	ΔE_{vdW}	ΔE_{elec}	ΔG_{gas}	ΔG_{solv}	ΔG_{bind}
ZIKV NS3 Helicase	-3546.66 ± 28.91	- 30102.45 ± 107.82	-33649.11 ± 103.65	-4466.57 ± 89.33	-38115.68 ± 48.08
NITD008 (Pose 4)	-5.86 ± 0.44	12.17 ± 4.43	6.31 ± 4.48	-28.40 ± 2.23	-22.09 ± 3.39
Complex	-27.60 ± 3.22	-25.88 ± 6.98	-53.48 ± 6.59	29.49 ± 4.00	**-23.99 ± 4.06**

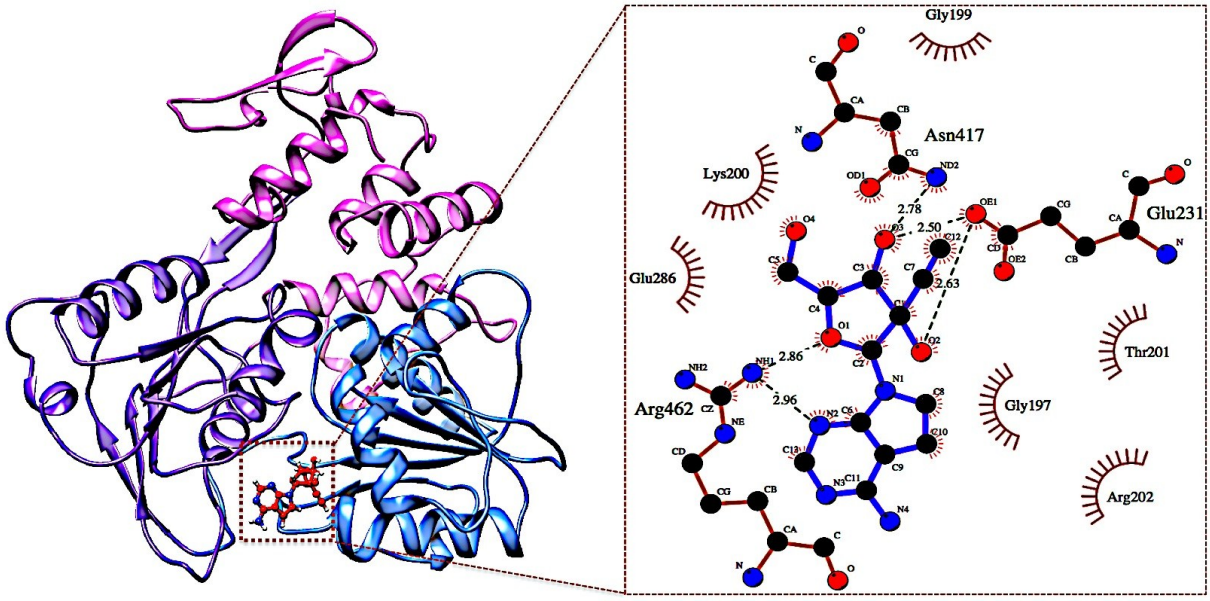

Figure S5: Complex of NITD008- NS3 Helicase with a Docking score of -7.1 kcal/mol. MM/GBSA calculations yielded a result of -23.99 kcal/mol. This pose showed the same docking score as the above ligand, however, three residues: Arg462, Asn417, and Glu231, were involved in stabilizing hydrogen bonds.

Energy Components (kcal/mol)					
	Δ E_{vdW}	**ΔE_{elec}**	**ΔG_{gas}**	**ΔG_{solv}**	**ΔG_{bind}**
ZIKV NS3 Helicase	-3541.38 ± 29.25	- 29907.78 ± 118.22	-33449.15 ± 118.80	-4626.31 ± 114.92	-38075.46 ± 56.93
NITD008 (Pose 5)	-5.54 ± 0.70	12.28 ± 5.43	6.74 ± 5.32	-26.45 ± 2.46	-19.71 ± 4.02
Complex	-13.69 ± 3.83	-7.75 ± 6.43	-21.44 ± 7.73	15.54 ± 5.95	**-5.90 ± 3.06**

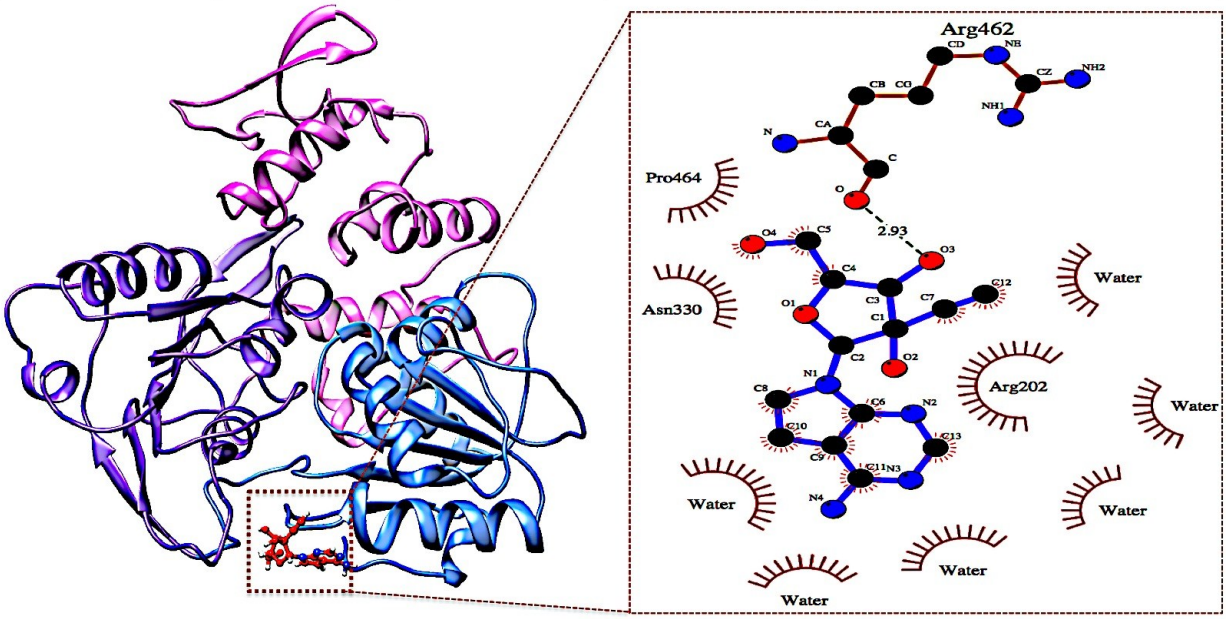

Figure S6: MM/GBSA calculations yielded a result of -5.90 kcal/mol, which was lower than that of the docking score of 6.9 kcal/mol. This was due to the ligand binding out of the active site of the enzyme, thus leading to minimal intermolecular forces at the hydrophobic pocket.