Mitoxantrone dihydrochloride, an FDA approved drug, binds with SARS-CoV-2 NSP1 C-terminal

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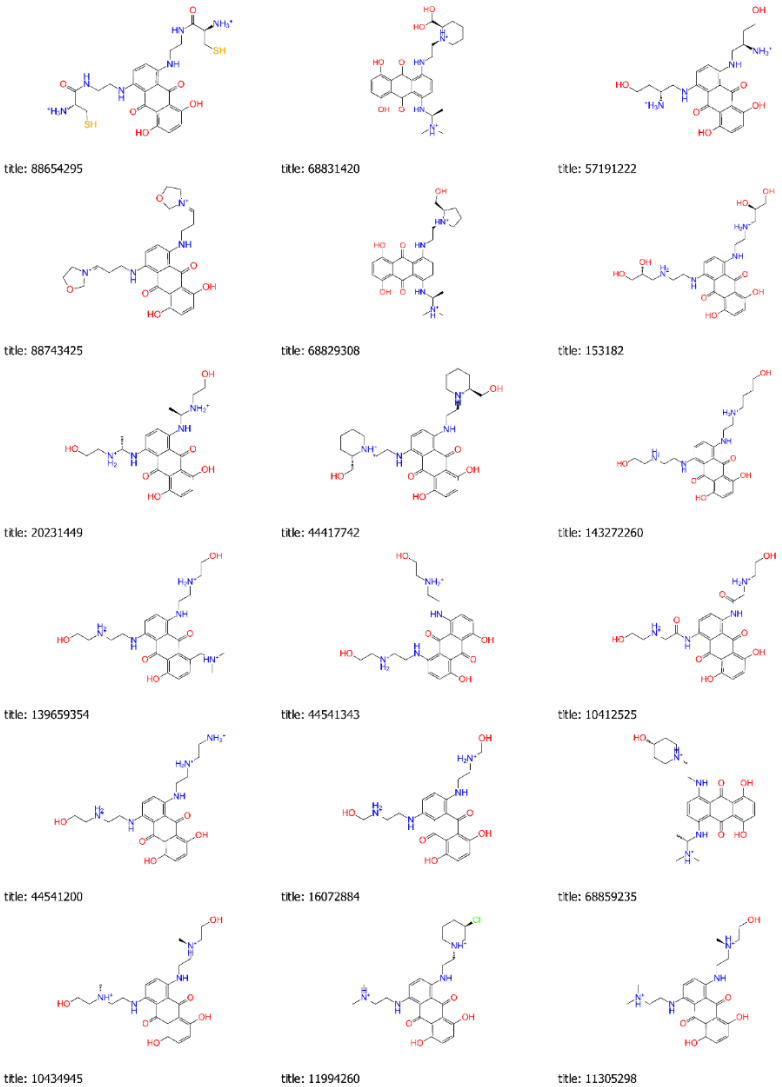
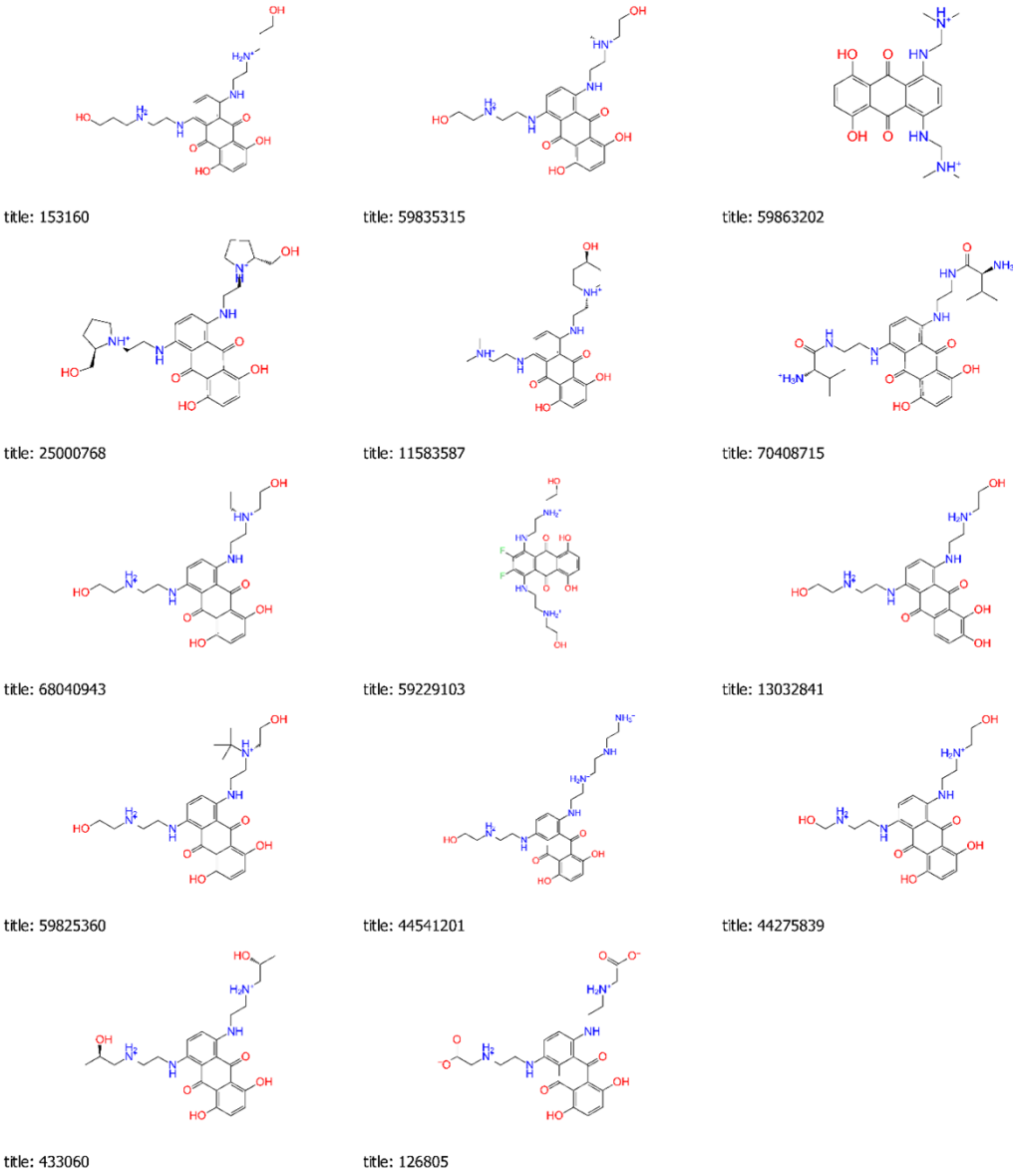
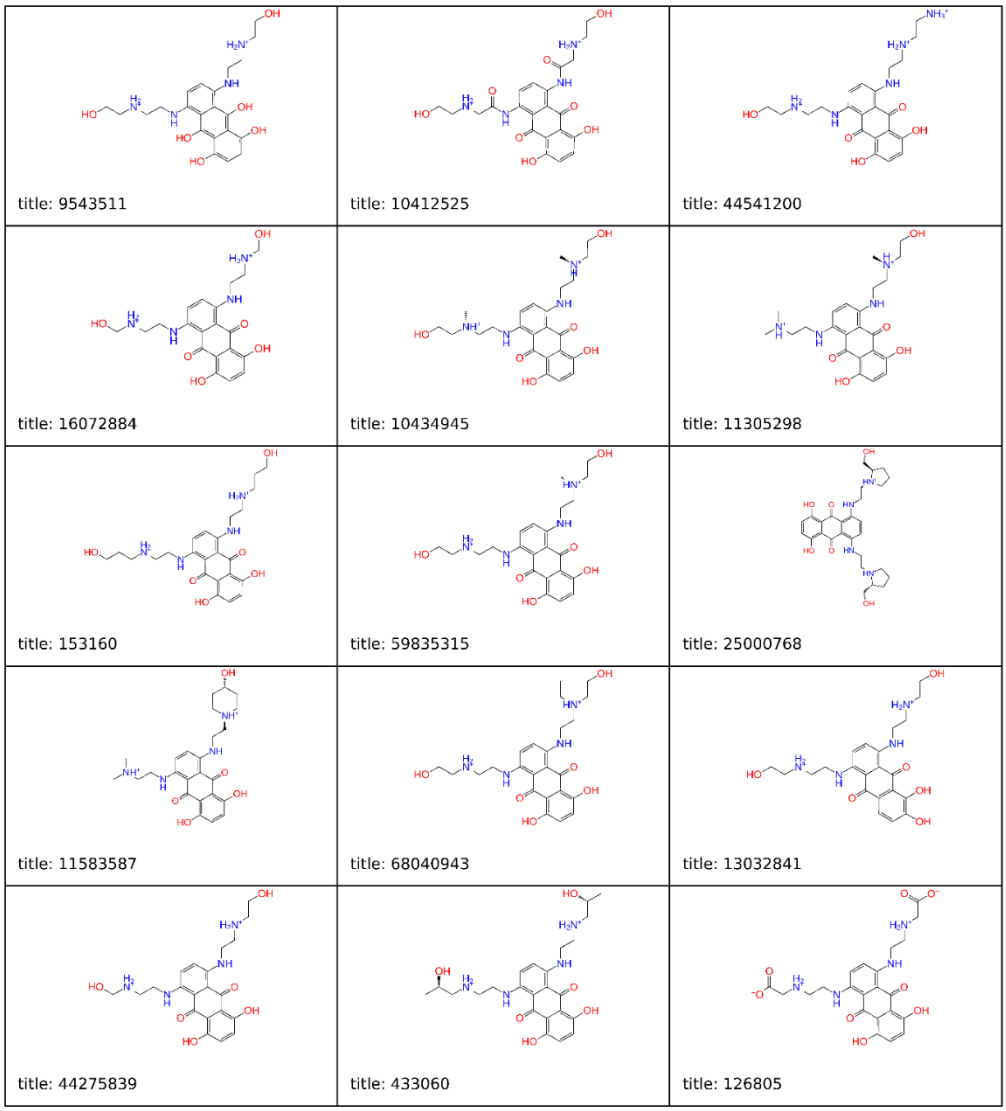
Supplementary Information



Supplementary Figure 1A: Two-dimensional structures of top identified compounds similar to Mitoxantrone from PubChem database with docking score more than -5.3 kcal/mol.

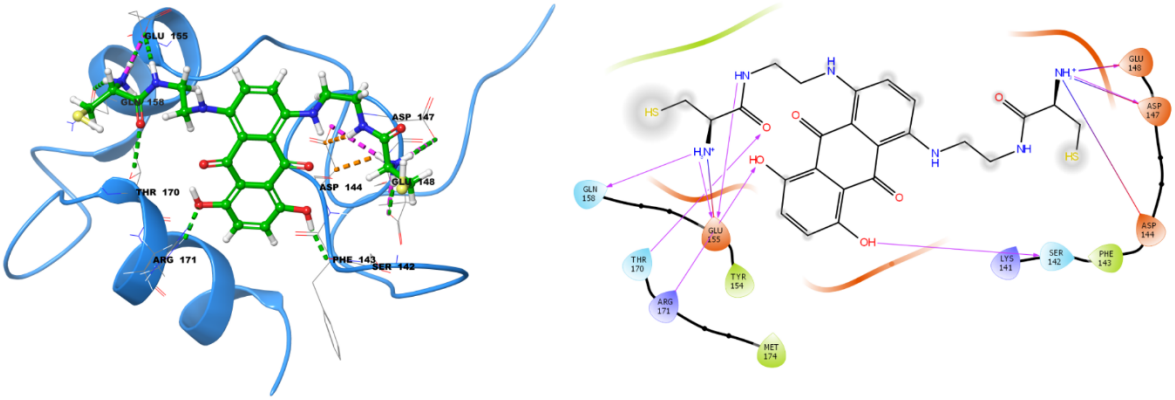


Supplementary Figure 1B: Two-dimensional structures of top identified compounds similar to Mitoxantrone from PubChem database with docking score more than -5.3 kcal/mol.

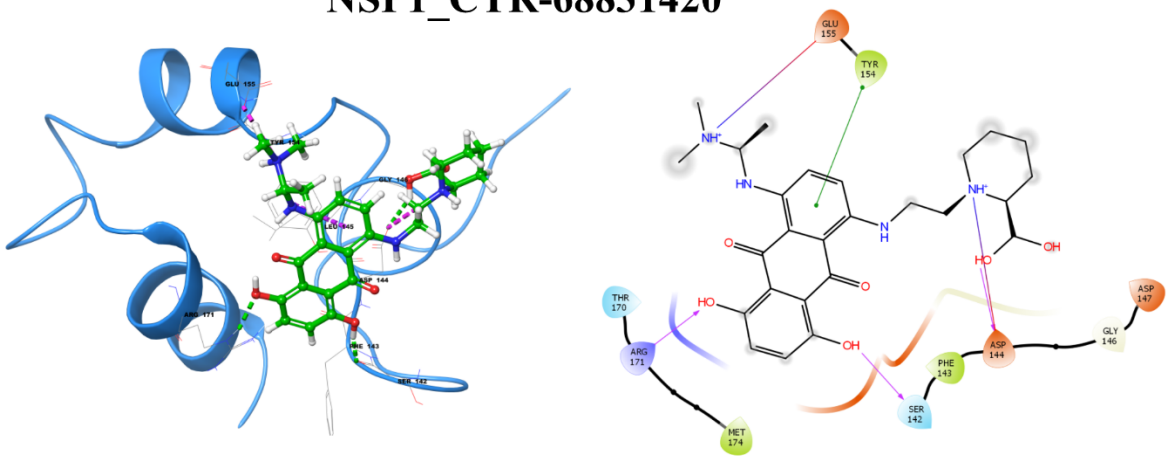


Supplementary Figure 2: Two-dimensional structures of top identified conformers similar to Mitoxantrone from PubChem database with docking score more than -5.3 kcal/mol.

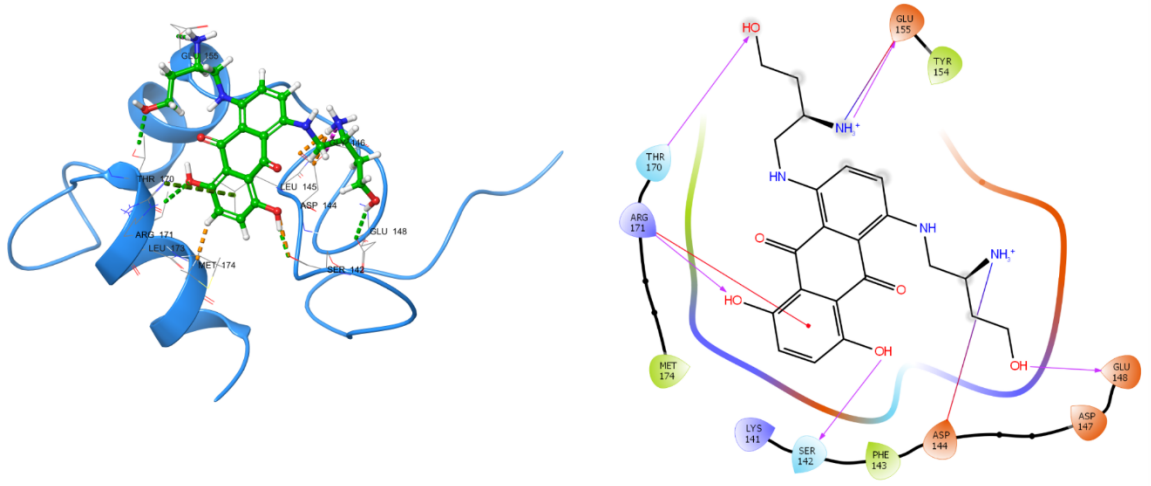
NSP1_CTR-88654295



NSP1_CTR-68831420

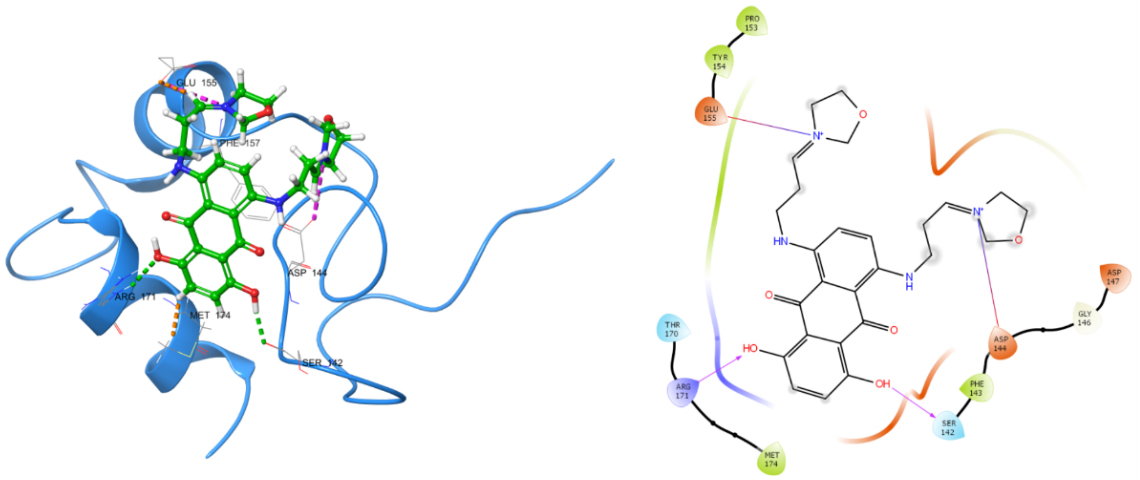


NSP1_CTR-57191222

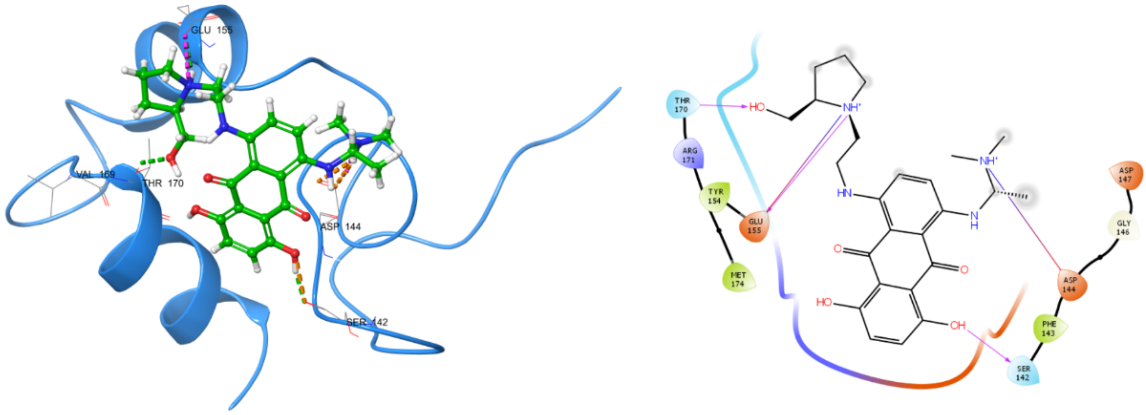


Supplementary Figure 3A: Three-dimensional binding poses and two-dimensional interaction diagrams of top identified compounds similar to Mitoxantrone from PubChem database with docking score more than -5.3 kcal/mol.

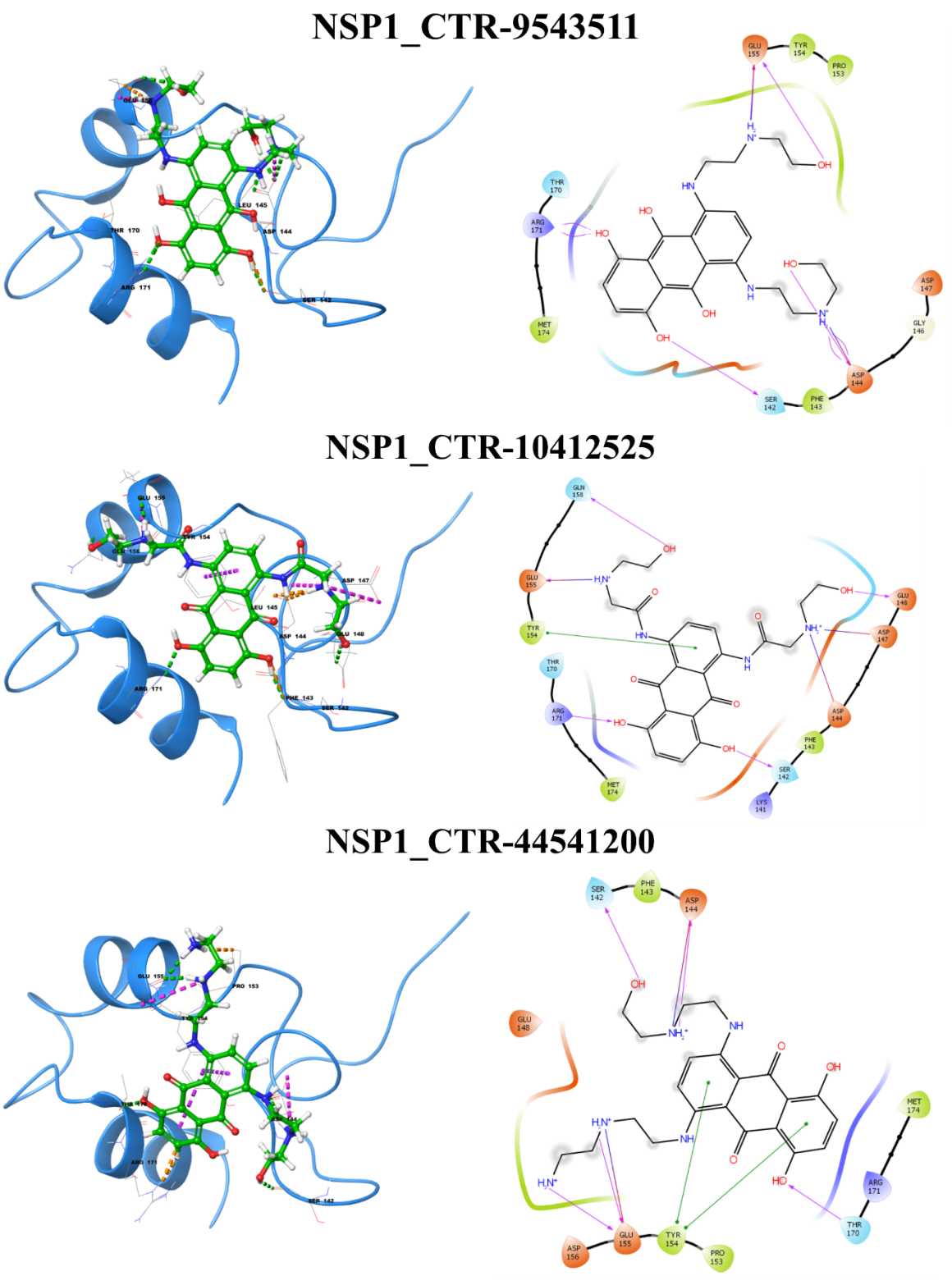
NSP1_CTR-88743425



NSP1_CTR-68829308

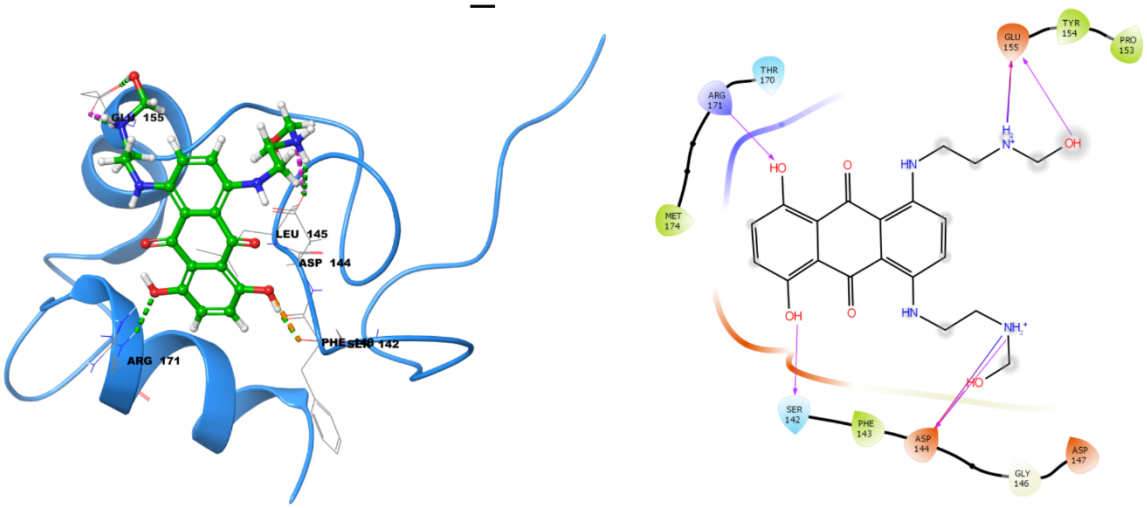


Supplementary Figure 3B: Three-dimensional binding poses and two-dimensional interaction diagrams of top identified compounds similar to Mitoxantrone from PubChem database with docking score more than -5.3 kcal/mol.

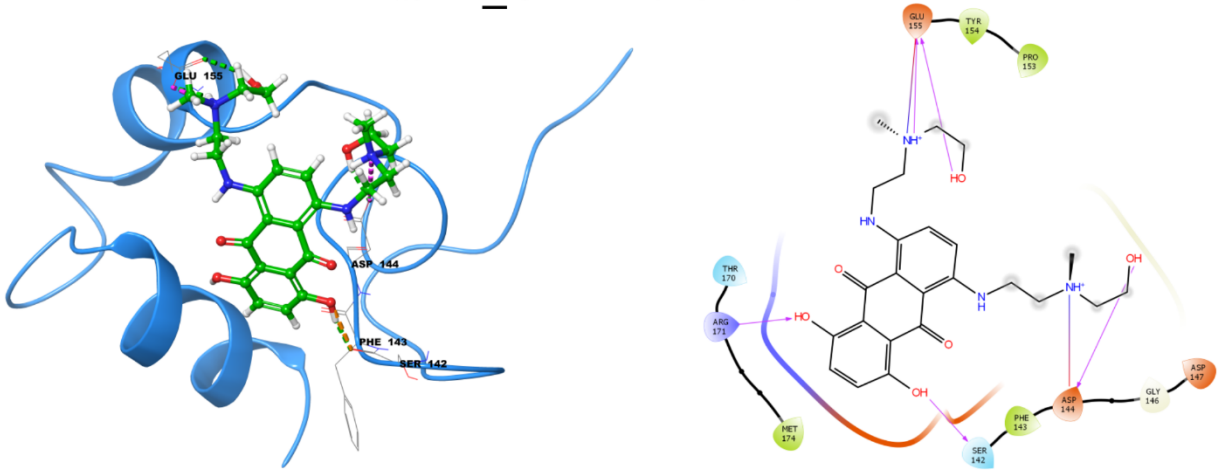


Supplementary Figure 4A: Three-dimensional binding poses and two-dimensional interaction diagrams of top identified conformers similar to Mitoxantrone from PubChem database with docking score more than -5.3 kcal/mol.

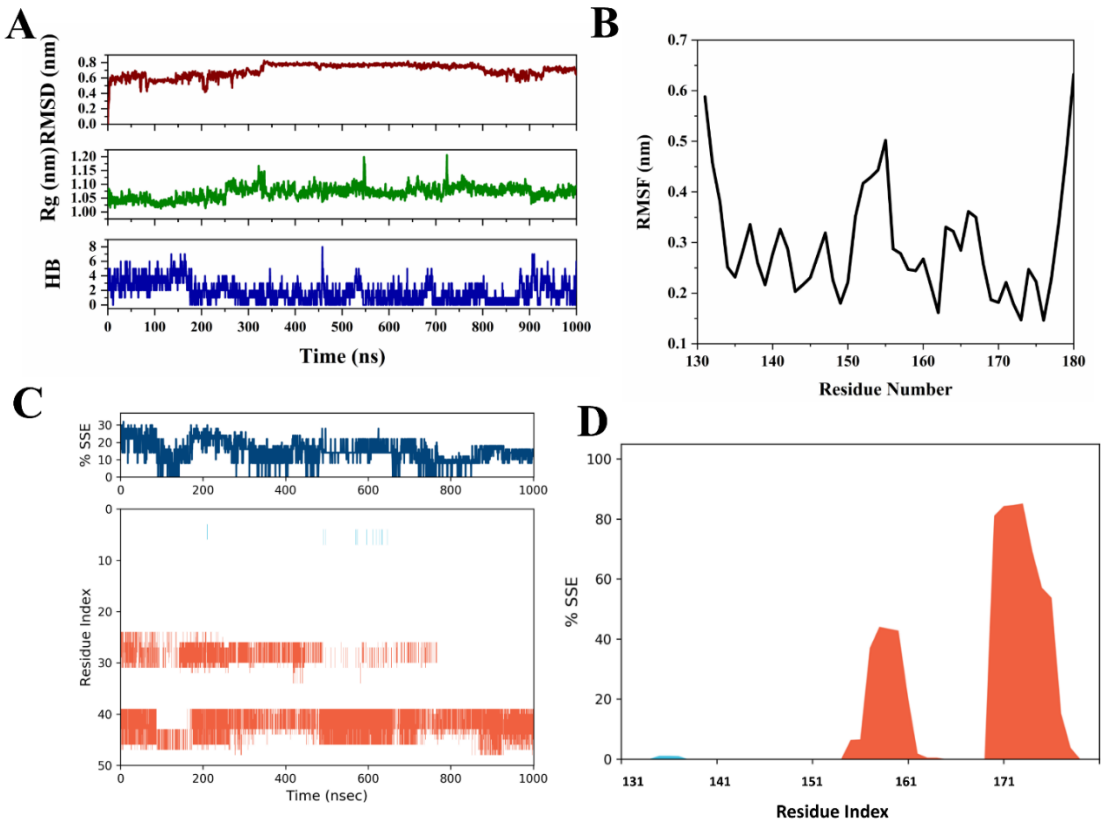
NSP1_CTR-16072884



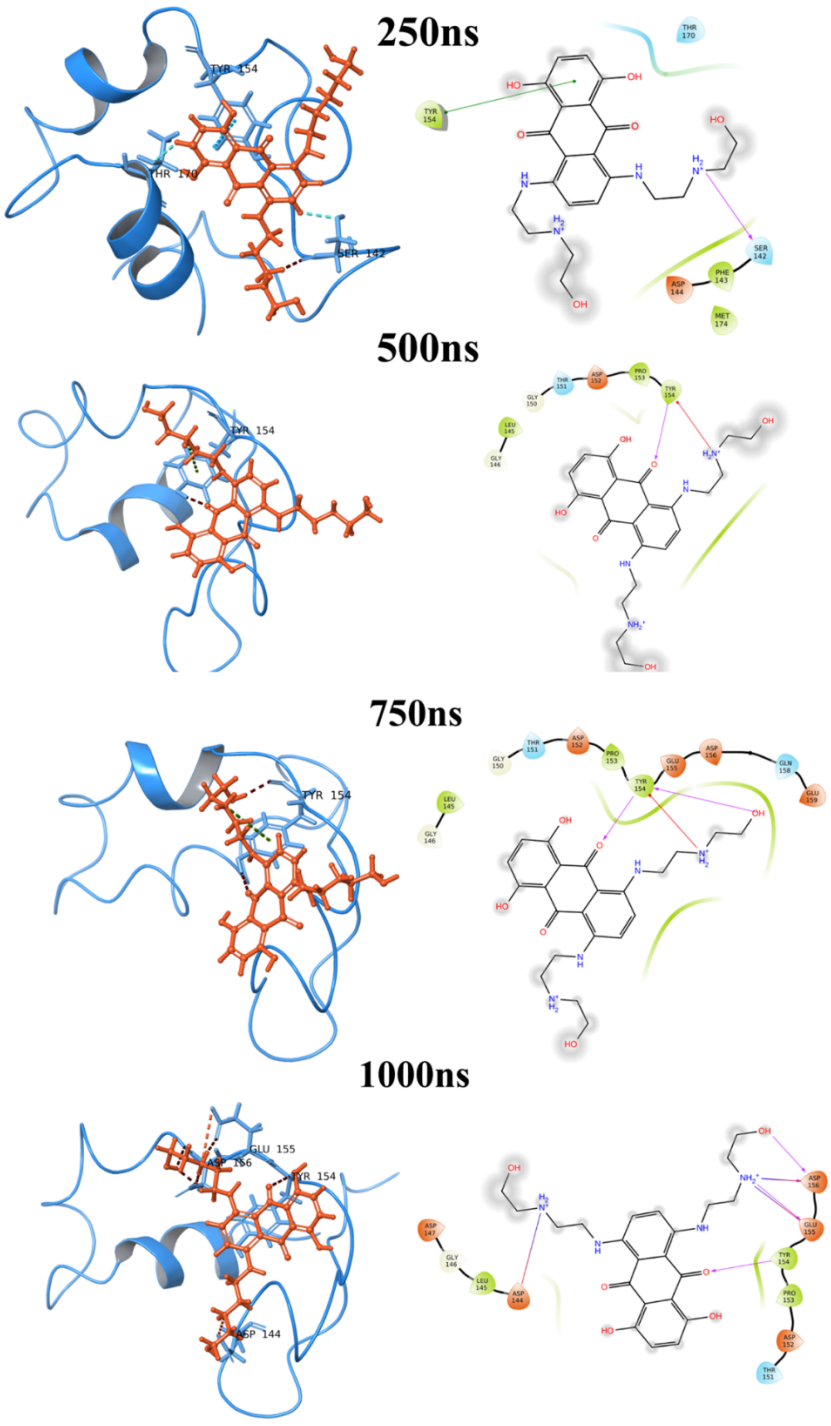
NSP1_CTR-10434945



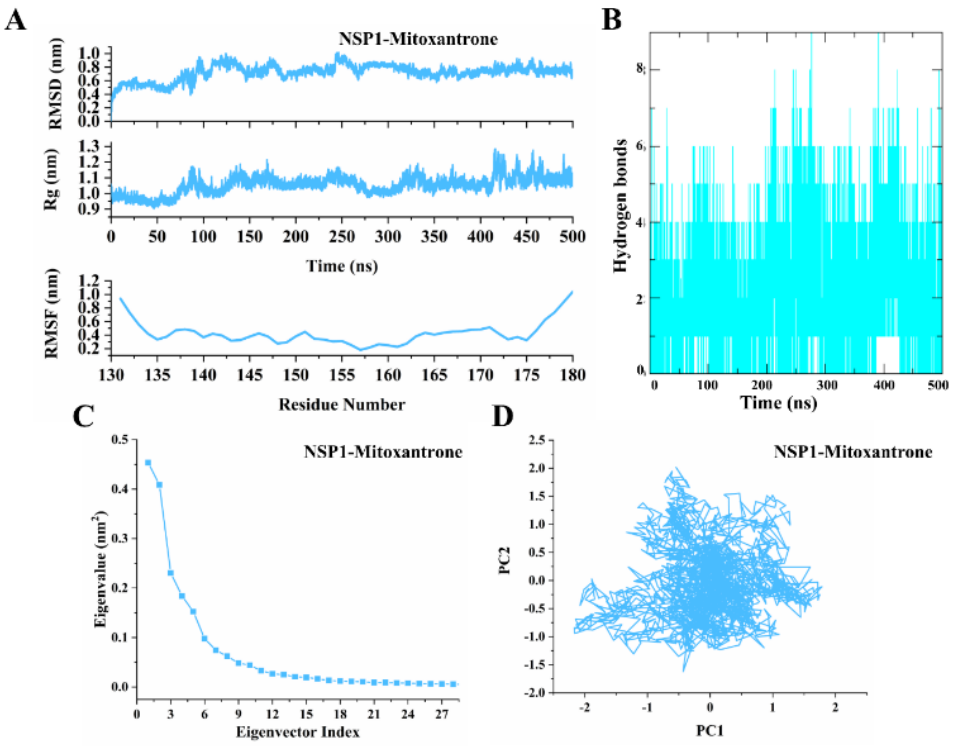
Supplementary Figure 4B: Three-dimensional binding poses and two-dimensional interaction diagrams of top identified conformers similar to Mitoxantrone from PubChem database with docking score more than -5.3 kcal/mol.



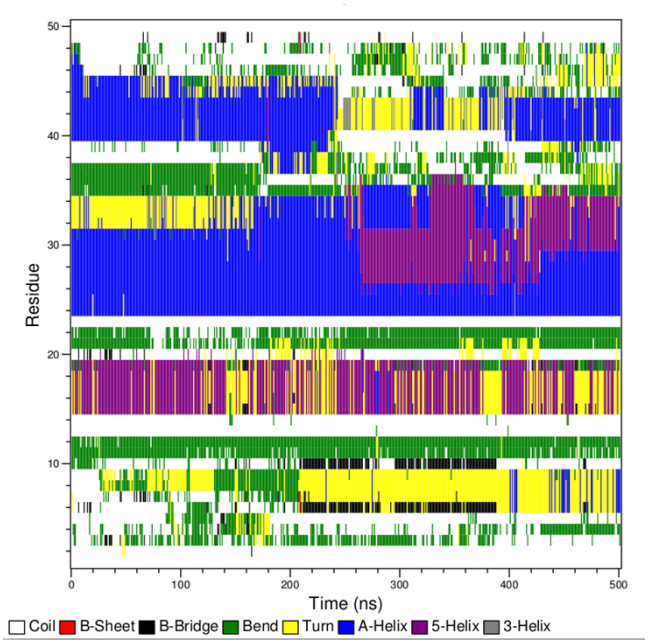
Supplementary Figure 5: Molecular dynamics simulation analysis of MTX bound NSP1-CTR using OPLS 2005 forcefield: (A) RMSD, Rg, of C-alpha (Cα) atoms and hydrogen bonds (from up to down), (B) RMSF analysis of C-alpha atoms, (C) Timeline representation of each residue of forming helical and beta sheets in respective frame of one microsecond long simulation trajectory. (D) Total secondary structure element (%SSE) is shown for each residue during entire simulation period. The orange color shows helical region and cyan shows the beta sheets.



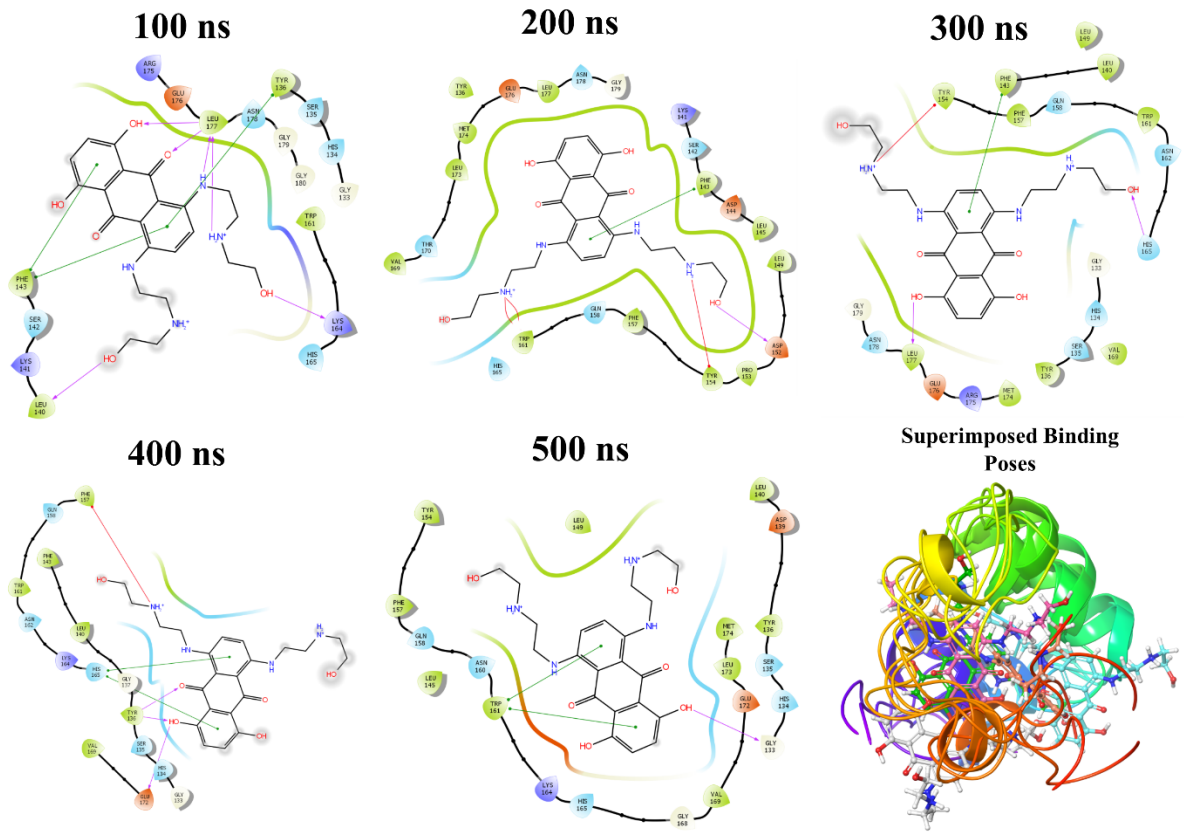
Supplementary Figure 6: Snapshots of NSP1-CTR and MTX complex from Desmond simulation trajectory: Three-dimensional binding poses and two-dimensional interaction diagrams are shown for captured frames at a regular interval of 250 ns.



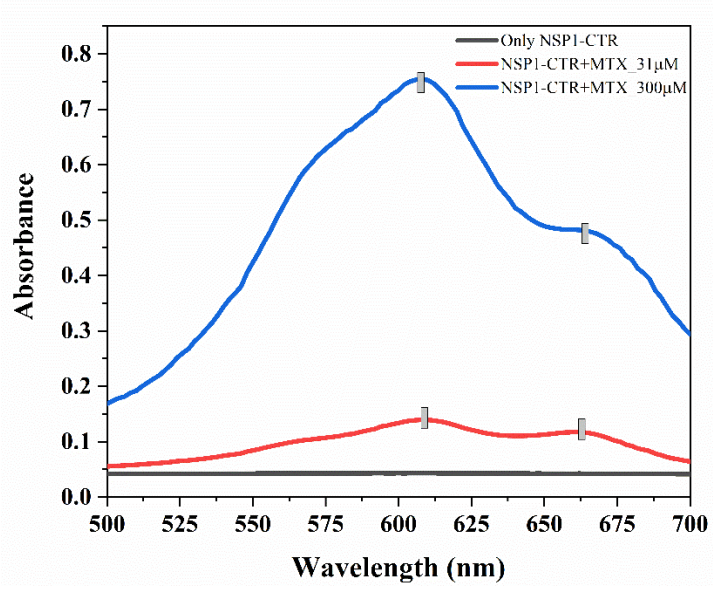
Supplementary Figure 7: Molecular dynamics simulation analysis of MTX bound NSP1-CTR using GROMOS 54A7 forcefield: (A) RMSD, Rg, and RMSF (from up to down), (B) hydrogen bonds analysis, (C) Eigenvector vs Eigenvalue plot, and (D) principal component analysis of last 20 ns simulation trajectory.



Supplementary Figure 8: Timeline representation of secondary structure change in NSP1-CTR during 500 ns long simulation trajectory. The colors are illustrated within the figure.



Supplementary Figure 9: Snapshots of NSP1-CTR and MTX complex from Gromacs simulation trajectory: Two-dimensional interaction diagrams are shown for captured frames at a regular interval of 100 ns. The corresponding three-dimensional poses are superimposed.



Supplementary Figure 10: Absorption spectra of NSP1-CTR in absence and presence of MTX at two concentrations (31 µM and 300 µM) representing two major peaks around 660 nm and 610 nm corresponding to monomer and dimer forms, respectively.

Supplementary Table 1: Detailed list of changes in τ_1, τ_2, and τ_3 components of tryptophan lifetime of NSP1 due to increasing concentration of mitoxantrone.

Mitoxantrone Concentration (μM)	$\tau_1 \pm s$ (ns)	$\tau_2 \pm s$ (ns)	$\tau_3 \pm s$ (ns)
0 (Only NSP1-CTR; 7.5 μM)	2.42 ± 0.10	0.61 ± 0.02	5.28 ± 0.04
25	2.31 ± 0.06	5.12 ± 0.06	0.63 ± 0.02
50	2.23 ± 0.08	5.02 ± 0.05	0.59 ± 0.02
100	2.26 ± 0.08	4.96 ± 0.06	0.62 ± 0.02
200	2.24 ± 0.08	4.91 ± 0.06	0.58 ± 0.01

Supplementary Table 2: Docking scores of top identified compounds similar to Mitoxantrone from PubChem database with docking score more than -5.3 kcal/mol.

S. No.	PubChem ID	Docking score (kcal/mol)	MM-GBSA (kcal/mol)
SC1	**88654295**	-6.93	-49.28
SC2	**68831420**	-6.66	-43.76
SC3	**57191222**	-6.34	-53.37
SC4	**88743425**	-6.17	-42.06
SC5	**68829308**	-6.10	-48.03
SC6	**153182**	-6.08	-54.47
SC7	**20231449**	-6.06	-43.61
SC8	**44417742**	-6.03	-48.63
SC9	**143272260**	-6.01	-52.19
SC10	**139659354**	-5.98	-56.79
SC11	**44541343**	-5.86	-50.88
SC12	**10412525**	-5.79	-57.66
SC13	**44541200**	-5.79	-45.10
SC14	**16072884**	-5.77	-47.02
SC15	**68859235**	-5.74	-40.43
SC16	**10434945**	-5.71	-43.93
SC17	**11994260**	-5.66	-32.52
SC18	**11305298**	-5.66	-46.99
SC19	**153160**	-5.65	-54.15
SC20	**59835315**	-5.59	-51.32

SC21	**59863202**	-5.56	-42.39
SC22	**25000768**	-5.54	-51.98
SC23	**11583587**	-5.53	-47.93
SC24	**70408715**	-5.53	-57.73
SC25	**68040943**	-5.53	-49.75
SC26	**59229103**	-5.44	-50.79
SC27	**13032841**	-5.43	-52.94
SC28	**59825360**	-5.43	-56.50
SC29	**44541201**	-5.43	-57.92
SC30	**44275839**	-5.39	-45.53
SC31	**433060**	-5.38	-48.97
SC32	**126805**	-5.35	-37.98

Supplementary Table 3: Docking scores of top identified conformers similar to Mitoxantrone from PubChem database with docking score more than -5.3 kcal/mol.

S. No.	PubChem ID	Docking score (kcal/mol)	MM-GBSA (kcal/mol)
SF1	**9543511**	-6.104	-51.061
SF2	**10412525**	-5.794	-57.658
SF3	**44541200**	-5.786	-45.099
SF4	**16072884**	-5.769	-47.023
SF5	**10434945**	-5.705	-43.93
SF6	**11305298**	-5.659	-46.986
SF7	**153160**	-5.647	-54.154
SF8	**59835315**	-5.589	-51.32
SF9	**25000768**	-5.535	-51.981
SF10	**11583587**	-5.534	-47.927
SF11	**68040943**	-5.527	-49.748
SF12	**13032841**	-5.426	-52.943
SF13	**44275839**	-5.389	-45.53
SF14	**433060**	-5.384	-48.973
SF15	**126805**	-5.348	-37.976

Supplementary Movie 1: Simulation trajectory of one microsecond long NSP1-CTR in complex with MTX using OPLS 2005 forcefield in Desmond simulation package.