Supplementary Information

Figure S1. Description of the optimal parameters of xK1 in physiological condition

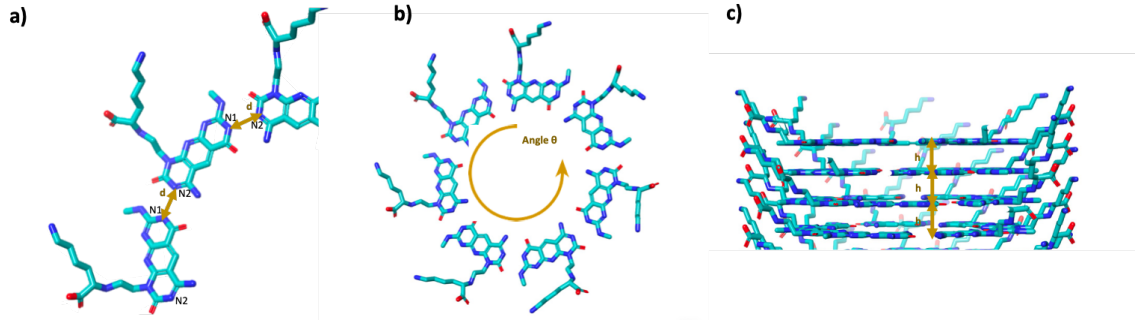

Figure S1a illustrates the distance (d) between the nitrogen atom N1 of the guanine in one motif and the nitrogen atom N2 of the cytosine in the other motif, measured at 2.95 Å. Figure S1b shows the rotational angle (θ) between successive rosette rings, which is -14.3°. Figure S1c depicts the vertical separation (h) between two stacked rosette rings, whether arranged in a stacked or helical configuration, measured at 3.35 Å. The xK1 structure was designed as right-handed stacked rosette nanotubes. The xK1 motif was manually constructed using the builder tool in Maestro and optimized concurrently. The optimized motif molecule was employed to form rosette rings, which were stacked to create a tubular structure comprising up to 10 rings. Ensuring optimal parameters is critical for maintaining the stability of the rosette nanotube under the designed conditions and preventing the complex system from blowing. These parameters were validated before incorporating xK1 with drug molecules to form the final complex systems.

Figure S2. Global Docking Results

Global Docking Results

CBL			CPT			DOX			FLU		
Pose Rank	Binding Energy (kcal/mol)	Binding Region	Pose Rank	Binding Energy (kcal/mol)	Binding Region	Pose Rank	Binding Energy (kcal/mol)	Binding Region	Pose Rank	Binding Energy (kcal/mol)	Bindi Regic
1	-3.49	LysR	1	-6.51	LysR	1	-3.58	LysR	1	-4.40	LysF
2	-3.46	LysR	2	-6.50	LysR	2	-3.57	LysR	2	-4.33	LysF
3	-3.38	LysR	3	-6.50	LysR	2	-3.57	LysR	2	-4.32	LysF
4	-3.28	LysR	3	-6.50	LysR	3	-3.56	LysR	4	-4.39	LysF
5	-3.20	LysR	4	-6.49	LysR	4	-3.52	LysR	5	-4.36	LysF
6	-3.19	LysR	4	-6.49	LysR	5	-3.49	LysR	5	-4.36	LysF
7	-2.88	LysR	4	-6.49	LysR	6	-3.37	LysR	6	-4.35	LysF
8	-2.74	LysR	5	-6.42	LysR	7	-3.46	LysR	7	-4.33	LysF
9	-2.63	LysR	6	-6.41	LysR	8	-3.37	LysR	8	-3.77	LysF
10	-2.61	LysR	7	-6.38	LysR	9	-2.91	LysR	9	-3.67	LysF

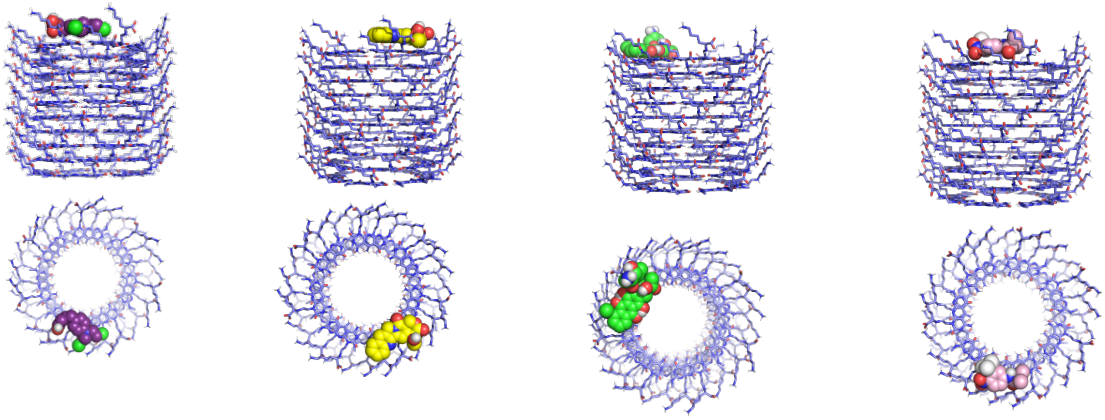

Figure S2 presents the global docking results of CBL, CPT, DOX, and FLU, respectively. Below the table are the figures of the top-ranked pose of each drug molecule against xK1 in front and top view.

Figure S3. Local Docking Results (LysL)

Local Docking Results (LysL)

CBL		CPT		DOX		FLU	
Pose Rank	Binding Energy (kcal/mol)	Pose Rank	Binding Energy (kcal/mol)	Pose Rank	Binding Energy (kcal/mol)	Pose Rank	Binding Energy (kcal/mol)
1	-2.88	1	-5.40	1	-2.78	1	-3.31
2	-2.64	1	-5.40	2	-2.71	2	-3.30
3	-2.43	1	-5.40	3	-2.49	3	-3.24
4	-2.17	2	-5.39	4	-2.26	4	-3.21
5	-2.15	2	-5.39	5	-2.24	4	-3.12
6	-2.06	2	-5.39	6	-1.64	4	-3.12
7	-2.07	2	-5.39	7	-1.54	5	-3.10
8	-2.03	2	-5.39	8	-1.50	5	-3.10
9	-1.99	2	-5.39	9	-1.29	6	-3.08
10	-1.91	3	-5.37	10	-1.27	7	-3.04

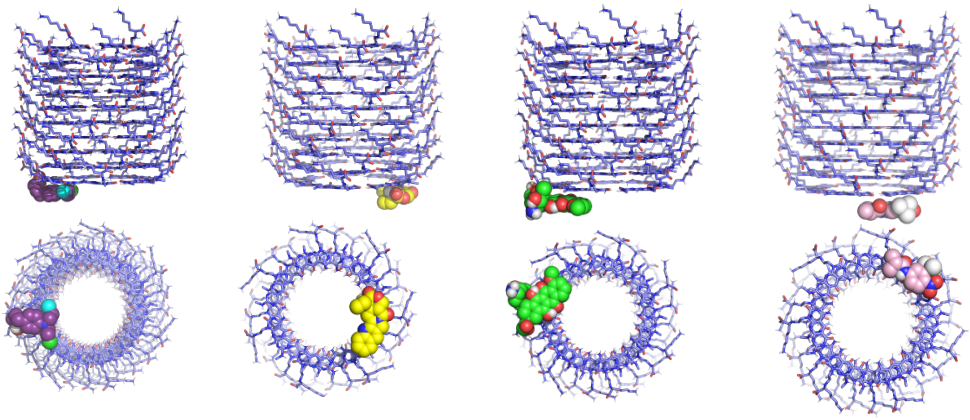

Figure S3 presents the local docking results at LysL binding site of CBL, CPT, DOX, and FLU, respectively. Below the table are the figures of the top-ranked pose of each drug molecule at the LysL of xK1 in front and top view.

Figure S4. Local Docking Results (Inner Channel)

Local Docking Results (Inner Channel)

CBL		CPT		DOX		FLU	
Pose Rank	Binding Energy (kcal/mol)	Pose Rank	Binding Energy (kcal/mol)	Pose Rank	Binding Energy (kcal/mol)	Pose Rank	Binding Energy (kcal/mol)
1	-3.11	1	-5.93	1	-1.47	1	-4.01
2	-2.91	1	-5.93	1	-1.47	2	-3.95
3	-2.89	2	-5.92	2	-1.43	3	-3.94
4	-2.82	2	-5.92	3	-1.40	4	-3.92
5	-2.81	3	-5.91	4	-1.34	5	-3.91
6	-2.68	4	-5.90	5	-1.32	6	-3.73
7	-2.63	5	-5.89	6	-1.31	7	-3.68
8	-2.57	6	-5.88	7	-1.26	8	-3.67
9	-2.53	7	-5.87	8	-1.24	9	-3.61
10	-2.52	7	-5.87	9	-1.14	9	-3.61

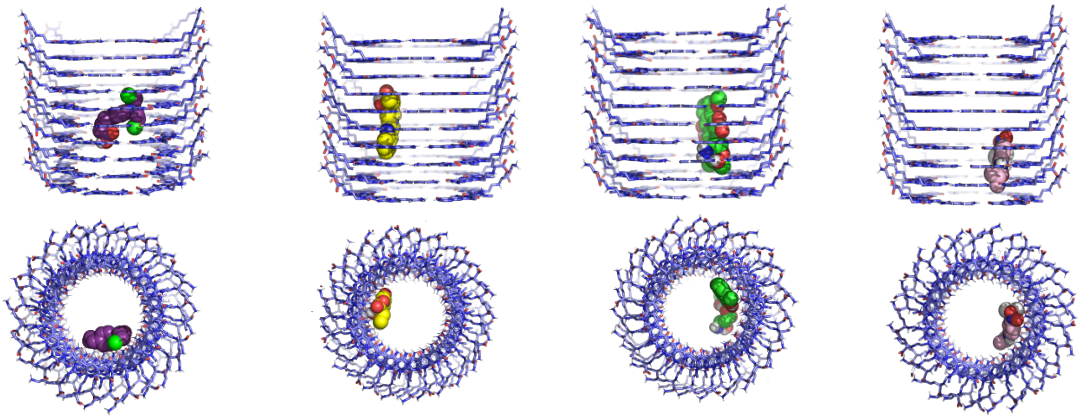

Figure S4 presents the local docking results in the inner channel binding site of CBL, CPT, DOX, and FLU, respectively. Below the table are the figures of the top-ranked pose of each drug molecule in the inner channel of xK1 in front and top view.

Figure S5. Protonated stabilized complexes

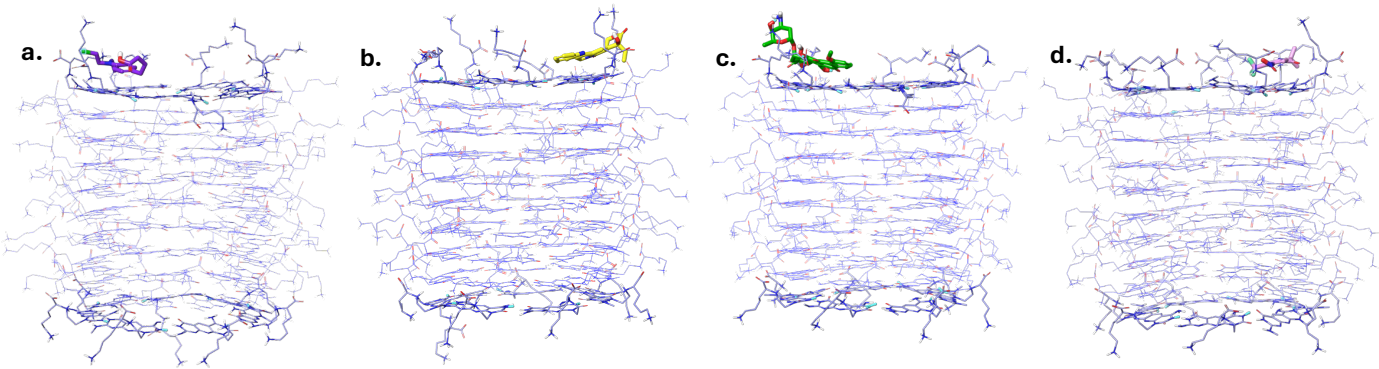

Figure S5 shows the protonated stabilized system of drug-xK1 complex. The emphasized motifs in darker blue are protonated. The termini regions of RNT are the only motifs that were protonated. The systems shown are a.) CBL, b.) CPT, c.) DOX, and d.) FLU when stabilized at LysR.

Figure S6. Radius of gyration analysis of CBL with xK1 in triplicate runs

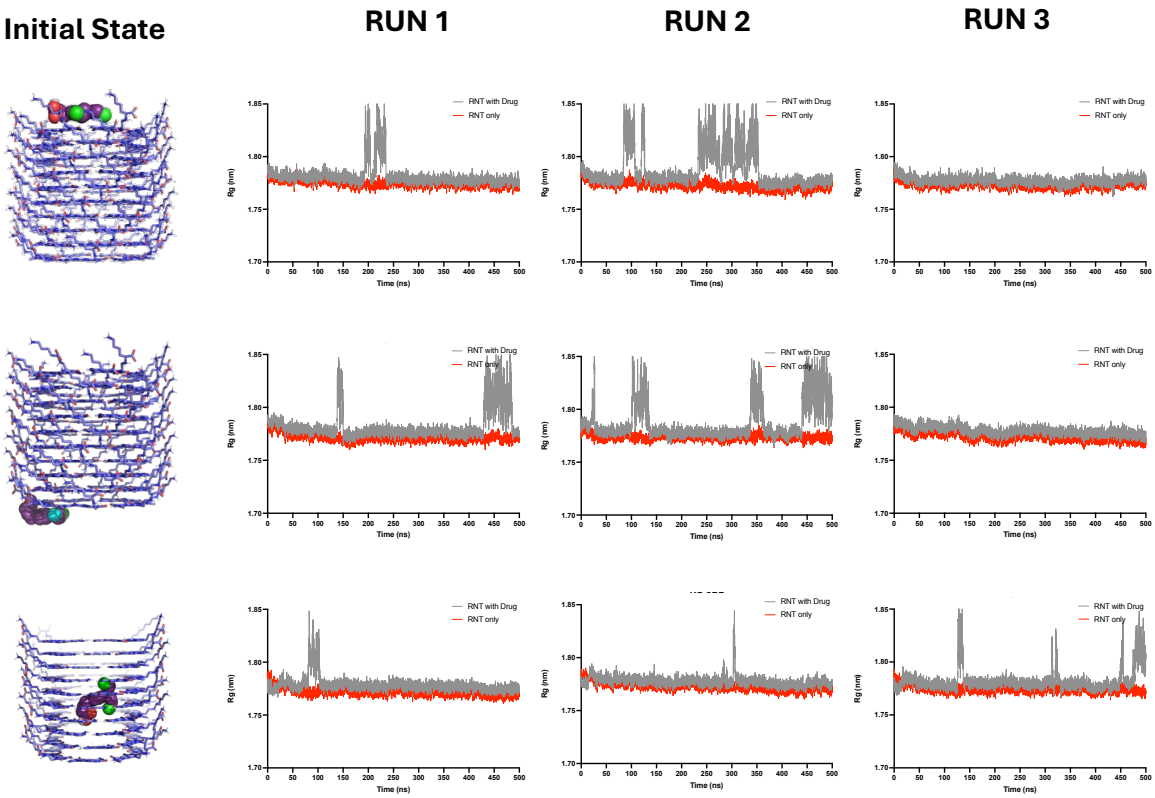

Figure S7. Radius of gyration analysis of CPT with xK1 in triplicate runs

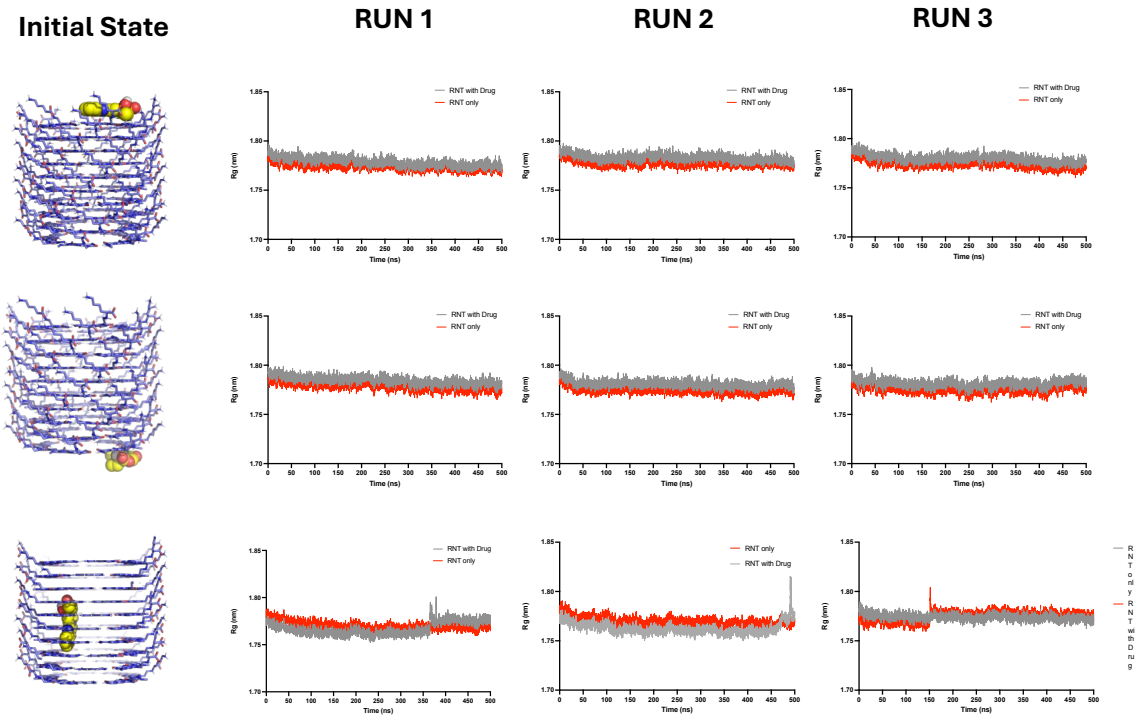

Figure S8. Radius of gyration analysis of DOX with xK1 in triplicate runs

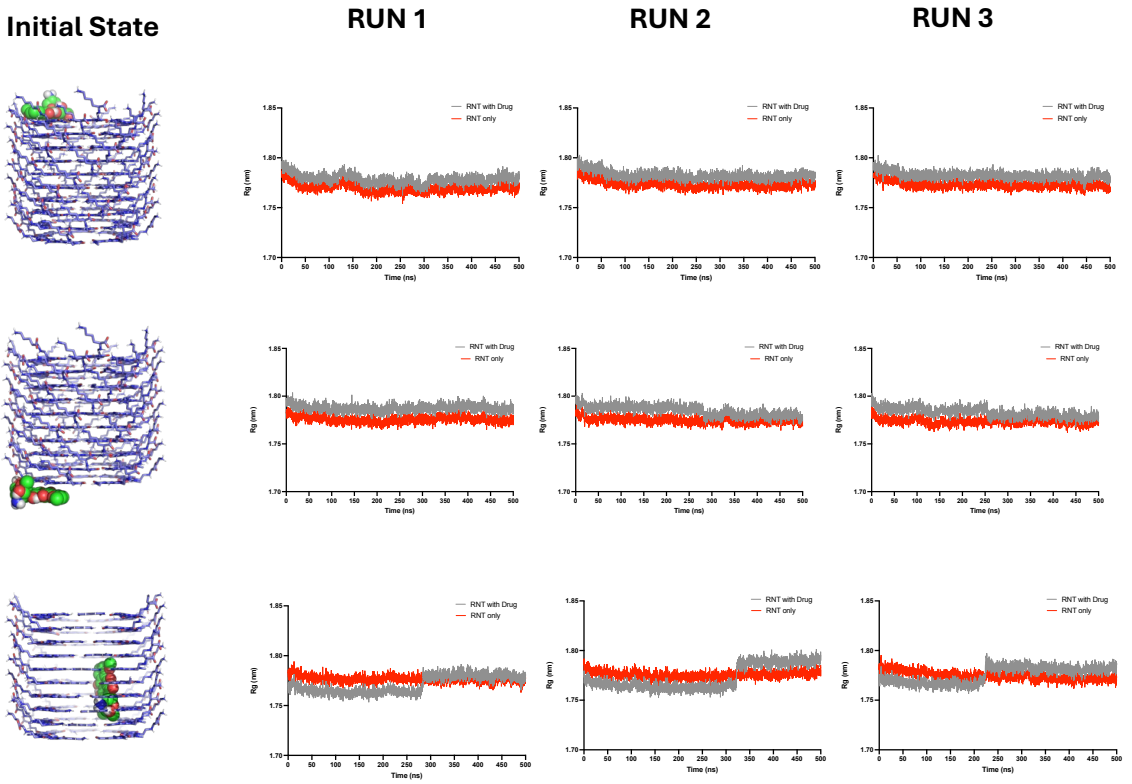

Figure S9. Radius of gyration analysis of DOX with xK1 in triplicate runs

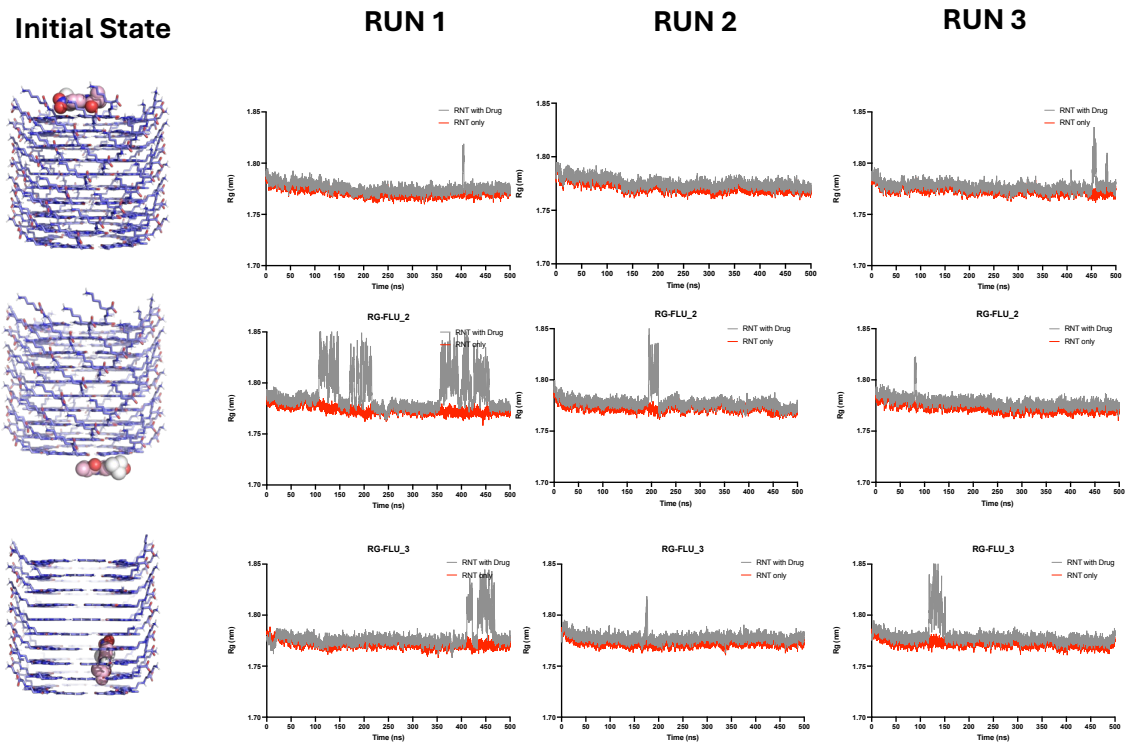

Figure S10. RMSD analysis of RNT alone for each complex

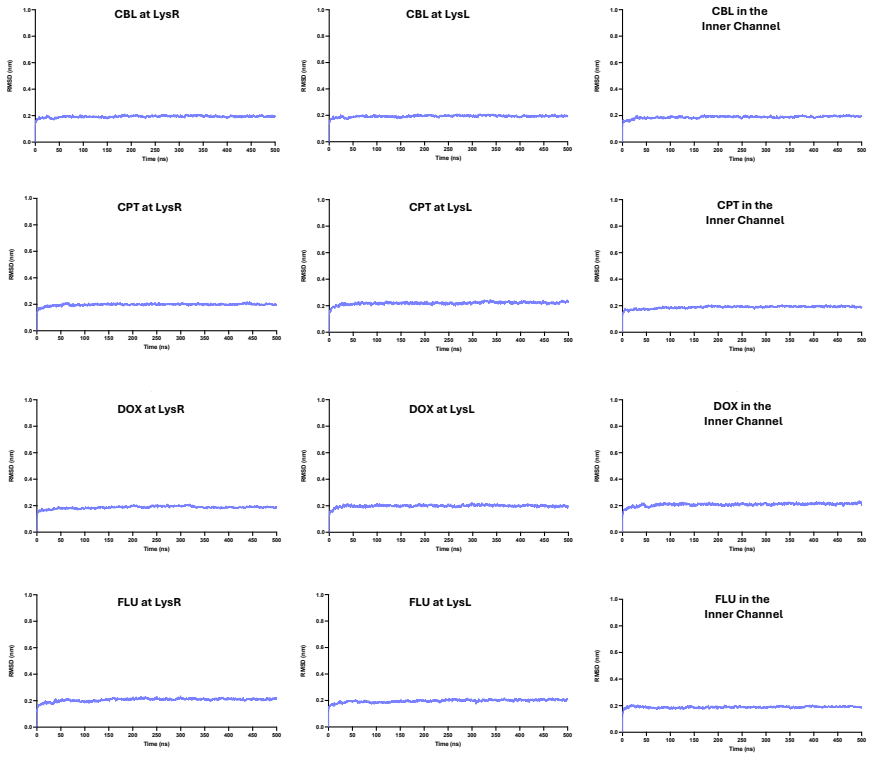

Figure S11. RMSD analysis of each drug