Supplementary Information to

"In Silico Study of the Synergistic Anti–Tumor Effect of Hybrid Topoisomerase–HDAC Inhibitors"

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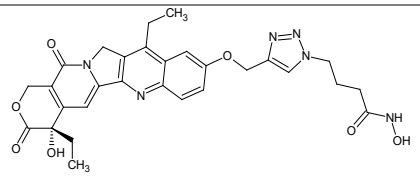
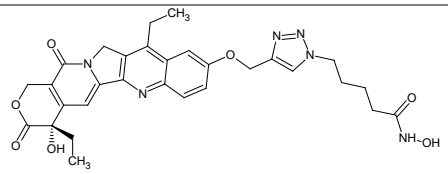
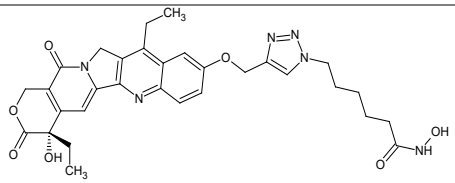
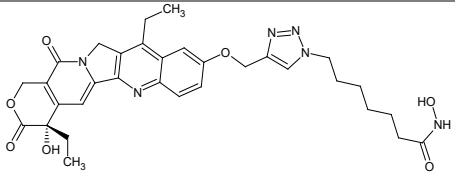
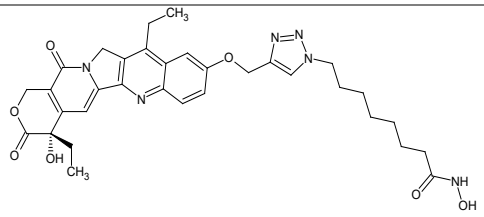
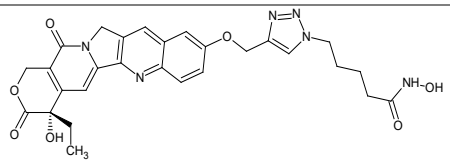
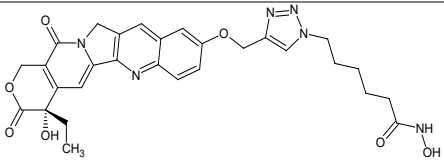
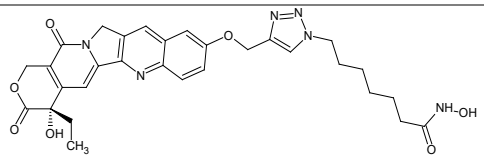
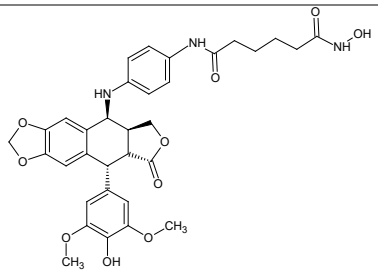
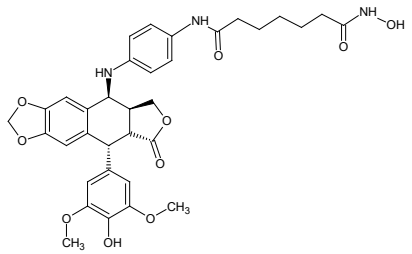
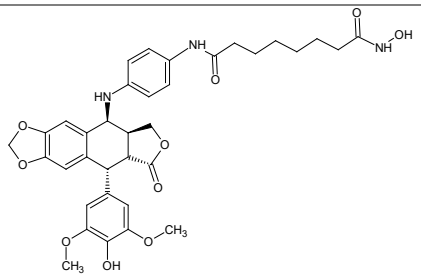
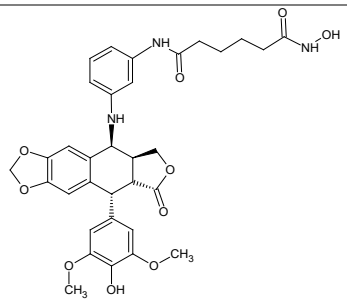
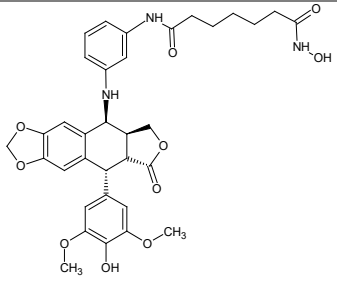
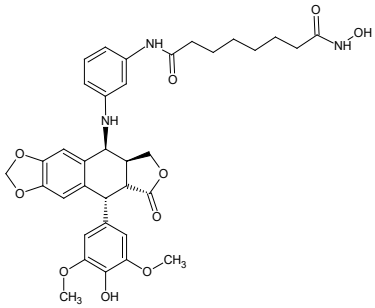
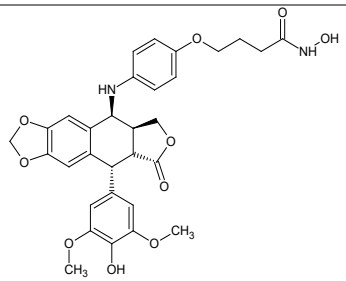
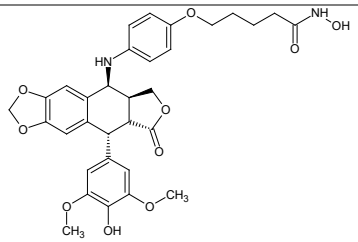
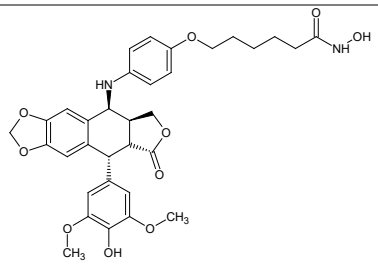
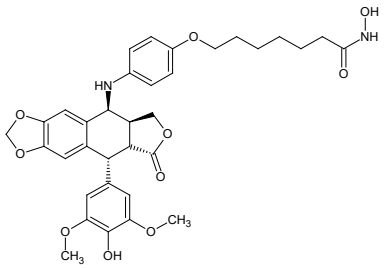
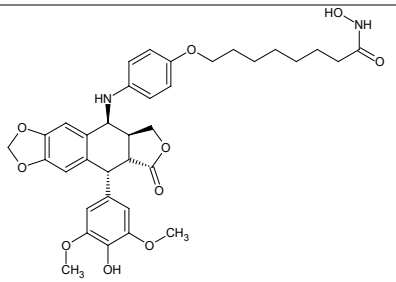
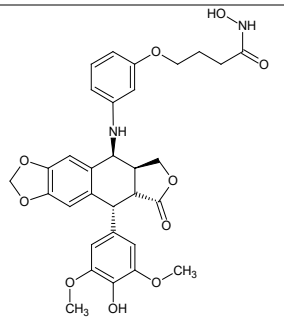
Table S1 2D structures and HDAC inhibition activities of the Top1-HDAC (C1-C8) and Top2-HDAC (P1-P21) hybrids

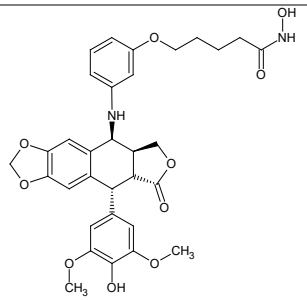
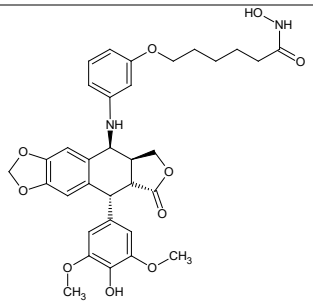
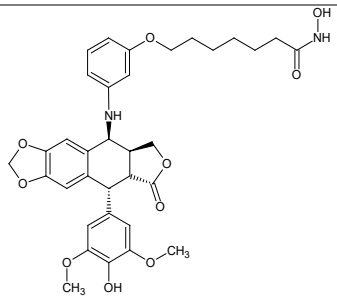
Ligand ID	Structure	HDAC1 IC_{50} (μM)	HDAC6 IC_{50} (μM)
C1		-	0.085
C2		-	-
C3		0.129	0.042
C4		0.05	0.036

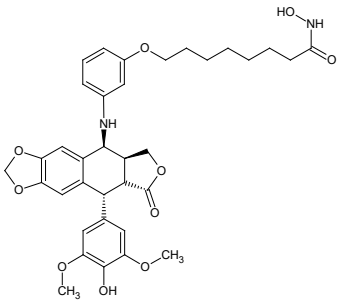
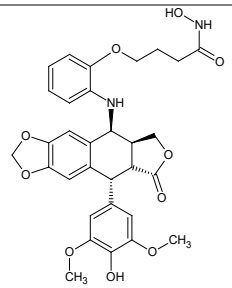
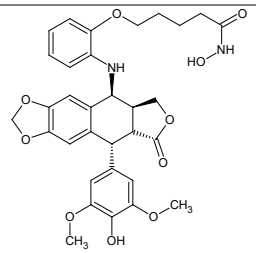
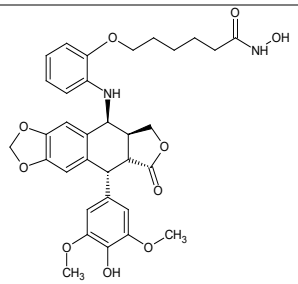
C5		0.369	0.075
C6		0.116	0.260
C7		-	-
C8		0.038	0.081
P1		2.83	1.06

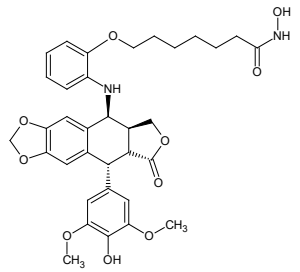
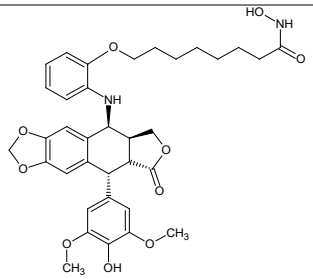
P2		0.59	0.13
P3		0.21	0.09
P4		1.43	0.52
P5		0.38	0.16

P6		0.10	0.04
P7		0.243	0.129
P8		0.125	0.088
P9		0.207	0.026

P10		0.029	0.016
P11		0.087	0.053
P12		0.385	0.405

P13		0.093	0.042
P14		0.045	0.015
P15		0.011	0.006

P16		0.039	0.069
P17		0.578	0.357
P18		0.369	0.084
P19		0.145	0.02

P20		0.072	0.027
P21		0.175	0.217

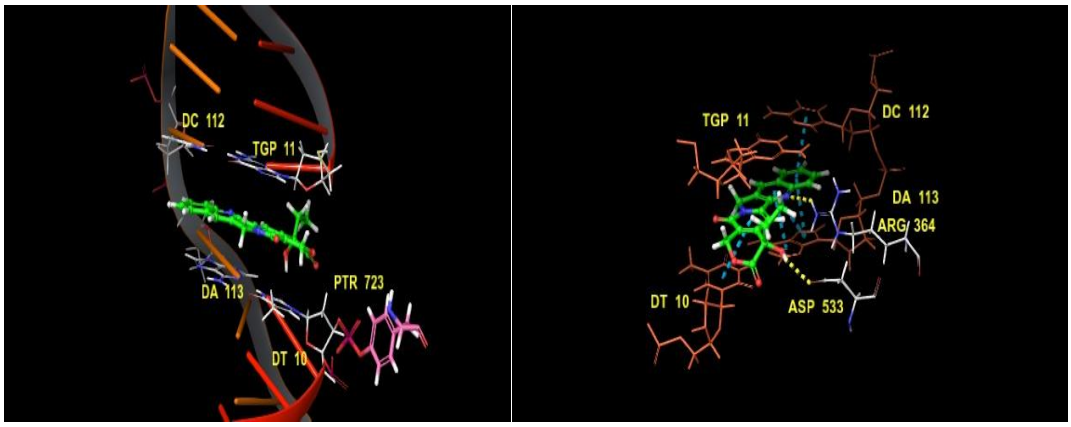


Fig. S1 Top1–DNA–CPT ternary complex showing single strand DNA break due to transesterification by Tyr723 (left). Interactions of CPT at Top1–DNA interface (right). Color scheme: –1/+1 nucleotides (orange), hydrogen bonds (yellow dashed lines), π–π stacking (cyan dashed lines), π–cation (green dashed lines).

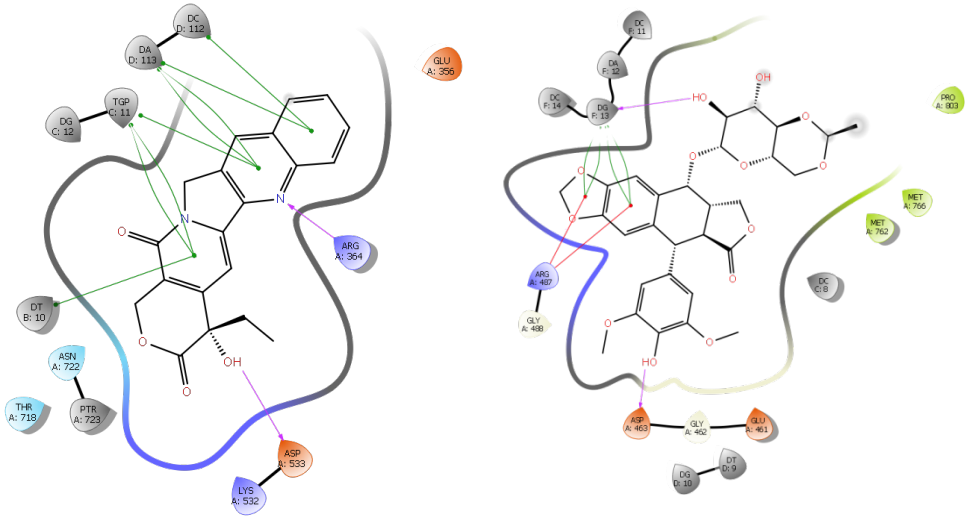


Fig. S2 2D Ligand interaction diagrams (LID) of camptothecin bound Top1-DNA complex (left) and etoposide-bound Top2-DNA complex (right). Colour scheme: Hydrogen bonds (purple arrows), π-π stacking interactions (green lines), π-cation interactions (red lines)

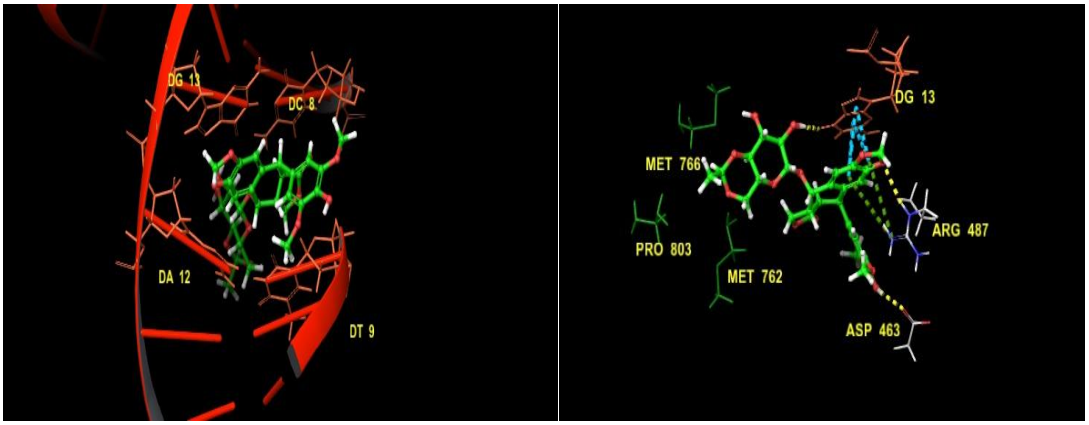


Fig. S3 Top2–DNA–etoposide ternary complex (left). Interactions of etoposide at Top2–DNA interface (right). Color scheme: –1/+1 nucleotides (orange), hydrogen bonds (yellow dashed lines), π–π stacking (cyan dashed lines), π–cation (green dashed lines).

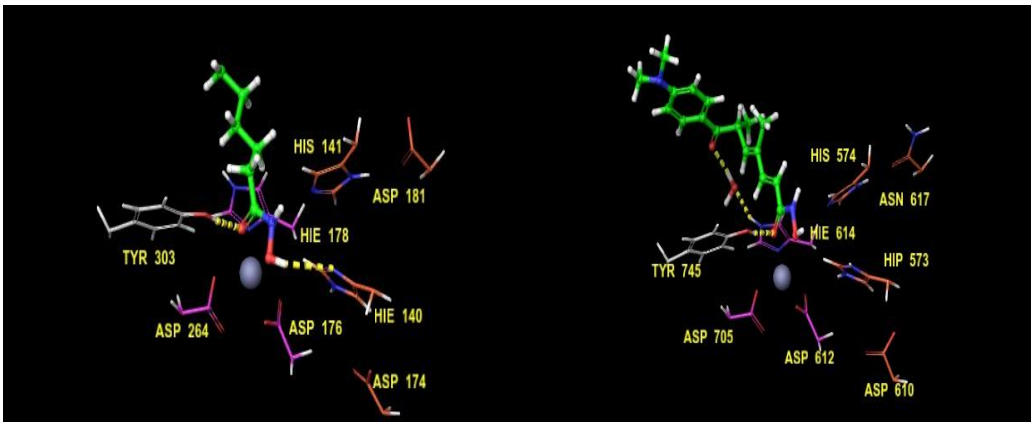


Fig. S4 Binding site and catalytically important residues of HDAC1 (left) and HDAC6 (right). Color scheme: Ligands (green carbons), zinc binding residues (pink carbons), charge relay dyads (orange carbons), hydrogen bonds (yellow dashed lines).

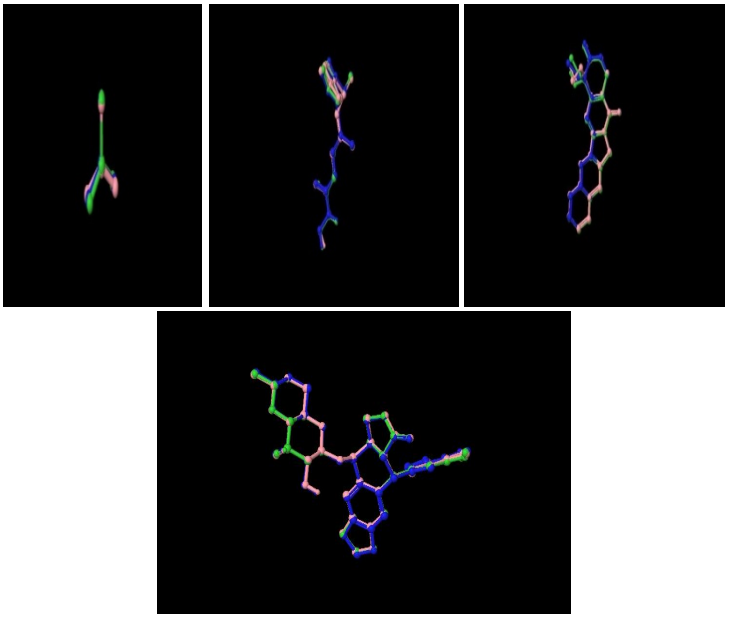


Fig. S5 Glide SP (green) and XP (blue) redocked ligand poses superimposed on co-crystal ligand poses (pink) of HDAC1 (PDB ID: *4BKX*), HDAC6 (PDB ID: *5WGI*), Top1-DNA complex (PDB ID: *1T8I*) and Top2-DNA complex (PDB ID: *5GWK*) (from left to right).

Table S2 RMSD values of Glide SP and XP redocked poses superimposed on co-crystal ligands.

	HDAC1	HDAC6	Top1-DNA	Top2-DNA
SP RMSD (Å)	0.2840	0.3288	0.8114	0.0956
XP RMSD (Å)	0.1409	0.3160	0.8629	0.1608

Table S3 XP docking parameters of Top1-HDAC hybrids (C1-C8) in Top1-DNA complex

ID	DS	E_{vdW}	E_{model}	Glide Energy	*HBond*	*Lipo-E_{vdW}*	*Electro*	*Penalties*	*H-bonds by C10 subst.*
CPT	-8.29	-54.06	-77.95	-57.31	-1.01	-7.70	-0.24	1.00	-
C8	-9.68	-72.45	-124.73	-82.28	-1.35	-7.64	-0.74	0.06	K436, dT9
C1	-8.87	-77.36	-138.15	-86.27	-2.51	-8.60	-0.67	5.05	K425, dC8
C6	-8.74	-72.44	-140.71	-83.03	-1.93	-8.48	-0.79	4.44	K425, dA113
C5	-8.62	-69.70	-138.47	-80.27	-1.83	-7.37	-0.79	1.51	K751, D440, dT10
C3	-8.10	-72.40	-158.69	-88.36	-1.85	-8.25	-1.20	5.00	Q421, K425, dA114
C4	-7.85	-82.01	-149.85	-92.14	-1.88	-8.96	-0.76	5.76	M428, Y426
C7	-6.71	-72.04	-146.96	-91.01	-2.80	-8.77	-1.42	6.04	S423, I424, K425, dA114
C2	-6.26	-74.68	-150.41	-92.71	-2.80	-8.51	-1.35	8.21	S423, I424, K425, dA114

Table S4 XP docking parameters of Top1-HDAC hybrids (C1-C8) in HDAC1 active site

ID	Tot Q	DS	GS	*E_{vdW}*	*E_{model}*	Glide energy	*HBond*	*Lipo-E_{vdW}*	*Electro*
C3	0	-7.8	-7.8	-46.4	-101.53	-71.02	-1.98	-3.75	-1.85
C5	0	-7.72	-7.72	-45.97	-73.07	-64.34	-2.42	-3.75	-1.38
C8	0	-7.23	-7.23	-52.6	-97.98	-69.8	-1.81	-3.8	-1.29
C6	0	-6.9	-6.9	-47.52	-88.97	-64.17	-2.25	-3.22	-1.25
C4	0	-6.85	-6.85	-49.11	-104.07	-72.72	-1.91	-3.85	-1.77
C7	-1	-6.59	-7.06	-45.55	-89.56	-70.35	-1.42	-3.56	-1.86
C2	0	-6.41	-6.41	-44.17	-90.22	-64.85	-1.32	-3.54	-1.55
C1	0	-6.39	-6.39	-39.37	-88.2	-60.09	-2.1	-2.77	-1.55
C5	-1	-6.27	-6.75	-37.25	-89.27	-63.32	-1.31	-3.26	-1.95
C7	0	-5.9	-5.9	-43.46	-84.3	-63.21	-1.66	-2.76	-1.48
C4	-1	-5.86	-6.34	-32.62	-73.34	-59.96	-0.89	-3.09	-2
C6	-1	-5.83	-6.31	-41.51	-76.38	-65.95	-1.35	-2.87	-1.83
C1	-1	-5.17	-5.63	-43.17	-91.25	-65.04	-1.01	-3.02	-1.64
C3	-1	-4.77	-5.24	-39.74	-86.12	-56.49	-1.08	-2.72	-1.26
C8	-1	-4.2	-4.67	-37.54	-82.26	-60.46	-0.88	-3.02	-1.72
C2	-1	-2.65	-5.86	-32.87	-75.99	-52.43	-1.66	-2.49	-1.47

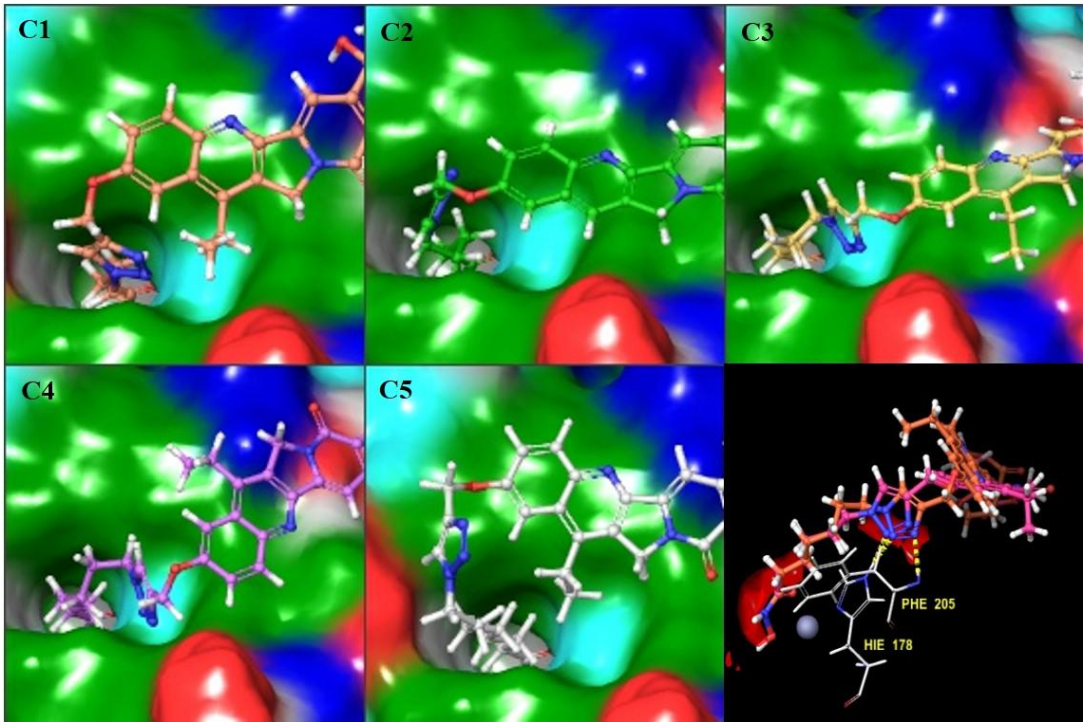


Fig. S6 Surface interactions of C1–C5 hybrids with HDAC1 and hydrogen bonds made by the triazole linker (bottom right). Surface colored as per residue property: hydrophobic (green), positively charged (blue), negatively charged (red), polar uncharged (cyan).

Table S5 XP docking parameters of Top1-HDAC (C1-C8) hybrids in HDAC6 active site

ID	Tot Q	DS	GS	E_{vdW}	E_{model}	Glide energy	*HBond*	*Lipo-*E_{vdW}	*Electro*
C2	0	-7.3	-7.3	-44.09	-87.26	-64.81	-2.2	-3.32	-1.55
C6	0	-6.8	-6.8	-45.83	-84.63	-65.29	-2.06	-3.31	-1.46
C4	0	-6.73	-6.73	-39.31	-69.13	-60.83	-2.29	-2.87	-1.61
C1	0	-6.45	-6.45	-33.89	-82.4	-50.5	-2.16	-2.78	-1.25
C3	-1	-5.96	-6.43	-36.12	-74.24	-60.63	-1.48	-3.13	-1.84
C3	0	-5.91	-5.91	-37.43	-75.01	-53.28	-2.05	-2.99	-1.19
C7	0	-5.76	-5.76	-40.31	-84.74	-62.38	-2.62	-2.89	-1.66
C5	-1	-5.68	-6.17	-34.26	-62.8	-56.52	-1.37	-3.01	-1.67
C8	-1	-5.51	-5.98	-30.76	-57.21	-51.49	-1.21	-2.81	-1.55
C1	-1	-5.48	-5.94	-37.41	-79.04	-63.28	-1.03	-2.97	-1.94
C7	-1	-5.47	-5.95	-35.35	-75.71	-57.1	-1.15	-2.9	-1.63
C6	-1	-5.39	-5.86	-40.51	-75.15	-63.09	-1.11	-3.06	-1.69
C8	0	-5.02	-6.37	-37.96	-64.82	-53.61	-2.6	-2.73	-1.17
C5	0	-4.71	-4.71	-33.8	-53	-43.23	-2.19	-1.81	-0.71
C4	-1	-3.01	-6.23	-40.44	-79.17	-61.71	-1.36	-3.11	-1.59
C2	-1	-2.99	-6.21	-31.26	-67.58	-53.7	-2.18	-2.23	-1.68

Table S6 XP docking parameters of Top2-HDAC (P1-P21) hybrids in the Top2-DNA complex

ID	Tot Q	DS	E_{vdW}	E_{model}	Glide energy	*HBond*	Lipo-E_{vdW}	*Electro*	Penalties
Etoposide	0	-9.70	-62.01	-114.89	-74.92	-2.52	-7.47	-0.97	1.00
P16	0	-13.70	-72.66	-181.77	-92.81	-3.72	-8.69	-1.51	0
P2	0	-13.56	-74.5	-168.85	-91.91	-4.1	-8.42	-1.31	0.08
P11	0	-13.28	-77.09	-180.35	-92.47	-3.66	-9.33	-1.15	0.64
P1	0	-13.22	-66.09	-161.02	-85.62	-4.61	-8.29	-1.47	0.95
P3	0	-13.1	-72.16	-194.04	-91.5	-4.05	-8.32	-1.45	0.52
P10	0	-12.86	-76.01	-168.77	-95.78	-4.07	-8.56	-1.48	1.04
P17	0	-12.67	-67.27	-142.56	-91.29	-3.05	-8.15	-1.8	0.15
P9	0	-12.59	-66.15	-159.85	-84.99	-4.39	-8.57	-1.41	1.59
P10	0	-12.36	-72.44	-143.83	-86.58	-2.87	-8.85	-1.06	0.22
P1	0	-12.34	-71.28	-154.19	-85.93	-2.36	-9.1	-1.1	0.03
P8	0	-12.32	-68.99	-148.55	-83.93	-2.96	-8.47	-1.12	0.03
P12	0	-12.3	-70.67	-149.41	-88.53	-3.18	-8.19	-1.34	0.23
P21	0	-11.68	-70	-195.58	-93.15	-2.82	-8.29	-1.74	0.65
P5	0	-11.68	-77.48	-178.48	-94.34	-1.67	-8.96	-1.26	0.02
P13	0	-11.63	-67.67	-135.43	-80.32	-2.37	-8.5	-0.95	0
P4	0	-11.62	-76.55	-178.44	-93.28	-2.21	-8.39	-1.25	0.04
P19	0	-11.61	-70.32	-146.15	-91.9	-2.84	-8.37	-1.62	1.01
P2	0	-11.58	-74.17	-154.88	-87.55	-2.74	-8.09	-1	0
P18	0	-11.52	-68.77	-145.42	-92	-2.92	-8.06	-1.74	1.01
P8	0	-11.42	-50.15	-114.57	-64.01	-2.9	-7.69	-1.04	0.01
P1	0	-11.23	-69.49	-125.75	-85.43	-2.27	-8.01	-1.2	0
P14	0	-11.15	-64.31	-146.54	-82.55	-2.52	-8.49	-1.37	1.02
P6	0	-11.13	-66.06	-143.78	-82.59	-1.79	-8.32	-1.24	0.01
P7	0	-11.01	-64.64	-129.74	-85.51	-1.61	-8.17	-1.57	0.09
P7	0	-10.72	-74.33	-142.79	-83.89	-2.85	-8.37	-0.72	1.03

Table S7 XP docking parameters of Top2-HDAC (P1-P21) hybrids in HDAC1 active site

ID	Tot Q	DS	GS	E_{vdW}	E_{model}	Glide energy	*HBond*	*Lipo-*E_{vdW}	*Electro*
P6	0	-8.03	-8.03	-43.25	-81.74	-62.58	-2.73	-3.63	-1.45
P9	0	-7.92	-7.92	-38.74	-94.97	-60.67	-2.65	-3.45	-1.65
P21	-1	-7.88	-8.02	-26.56	-76.56	-51.51	-1.44	-3.00	-3.37
P10	0	-7.78	-7.78	-42.11	-92.11	-61.97	-2.22	-3.70	-1.49
P10	-1	-7.73	-7.85	-35.7	-81.97	-58.34	-0.96	-2.93	-1.7
P13	-1	-7.59	-7.71	-32.8	-67.95	-57.36	-1.74	-3.01	-1.84
P1	0	-7.49	-7.49	-43.3	-84.29	-61.79	-2.49	-3.37	-1.39
P8	0	-7.46	-7.46	-39.81	-90.06	-64.74	-1.91	-3.52	-1.87
P19	0	-7.42	-7.42	-42.73	-82.44	-61.46	-2.08	-3.78	-1.41
P16	0	-7.4	-7.4	-42.48	-70.71	-59.89	-2.26	-3.44	-1.31
P21	0	-7.39	-7.39	-42.3	-86.18	-57.63	-2.18	-3.65	-1.15
P12	0	-7.37	-7.37	-47.92	-85.32	-66.17	-2.15	-3.92	-1.37
P14	0	-7.37	-7.37	-39.62	-76.58	-54.68	-2.28	-3.51	-1.13
P6	0	-7.36	-7.36	-42.27	-75.76	-66.74	-2.04	-3.26	-1.84
P5	0	-7.33	-7.33	-43.61	-88.91	-62.54	-2.29	-3.37	-1.42
P14	0	-7.31	-7.31	-29.59	-82.68	-55.26	-2.6	-2.68	-1.93
P21	-1	-7.29	-7.43	-25.64	-72.79	-50.29	-1.27	-2.78	-3.35
P20	0	-7.27	-7.27	-43.12	-68.75	-60.68	-2.24	-3.39	-1.32
P16	0	-7.25	-7.25	-42.35	-77.91	-59.97	-1.64	-3.89	-1.32
P6	0	-7.24	-7.24	-47.41	-97.5	-68.05	-2.01	-3.47	-1.55
P5	0	-7.15	-7.15	-44.07	-79.58	-63.22	-2.42	-3.23	-1.44
P20	0	-7.13	-7.13	-44.72	-69.99	-62.63	-1.84	-3.77	-1.34
P5	0	-7.12	-7.12	-44.29	-95.66	-64.42	-2.05	-3.4	-1.51
P18	0	-7.12	-7.12	-40.71	-81.63	-56.53	-2.29	-3.35	-1.19
P7	0	-7.1	-7.1	-43.65	-87.21	-56.41	-2.78	-3.33	-0.96
P15	0	-7.07	-7.07	-38.13	-75.07	-56.08	-2.24	-3.13	-1.35
P20	0	-7.06	-7.06	-40.46	-72.49	-57.67	-2.29	-3.28	-1.29
P11	0	-7.02	-7.02	-44.27	-80.45	-61.51	-1.45	-4.05	-1.29
P19	0	-7.02	-7.02	-40.4	-85.84	-56.77	-1.7	-3.6	-1.23
P11	-1	-7.02	-7.16	-18.69	-67.44	-43.44	-0.99	-2.79	-3.36
P5	0	-6.98	-6.98	-43.92	-78.67	-62.59	-2.47	-3.17	-1.4
P11	0	-6.98	-6.98	-45.03	-86.75	-58.57	-2.58	-3.22	-1.02
P15	0	-6.92	-6.92	-41.04	-80.28	-58.62	-2.29	-3.13	-1.32
P18	0	-6.86	-6.86	-45.47	-85.56	-60.27	-2.15	-3.66	-1.11
P20	0	-6.83	-6.83	-47.01	-81.46	-63.99	-1.6	-3.54	-1.27
P2	0	-6.83	-6.83	-42.19	-78.05	-58.07	-2.26	-2.96	-1.19
P4	0	-6.82	-6.82	-42.72	-81.59	-64.21	-1.92	-2.67	-1.61
P16	0	-6.81	-6.81	-35.73	-80.75	-62.37	-1.63	-2.68	-2
P4	-1	-6.8	-7.27	-27.53	-77.91	-53.33	-0.82	-2.77	-3.44
P9	0	-6.77	-6.77	-35.88	-82.34	-55.11	-1.81	-3.08	-1.44

Table S8 XP docking parameters of Top2-HDAC (P1-P21) hybrids in the HDAC6 active site

ID	Tot Q	DS	GS	E_{vdW}	E_{model}	Glide energy	*HBond*	*Lipo*	*Electro*
P15	0	-9.14	-9.14	-30.16	-69.79	-48.98	-2.64	-2.97	-1.41
P6	0	-9.1	-9.1	-40.22	-85.55	-64.1	-3.93	-3.1	-1.79
P6	0	-8.88	-8.88	-36.95	-88.8	-60.6	-3.9	-2.91	-1.77
P5	0	-8.87	-8.87	-37.76	-79.45	-64.09	-3.73	-2.97	-1.98
P6	0	-8.53	-8.53	-42.47	-91.25	-68.96	-2.79	-3.54	-1.99
P3	0	-8.29	-8.29	-40.32	-86.59	-61.39	-3.67	-3.1	-1.58
P5	0	-8.29	-8.29	-38	-79.7	-60.1	-3.22	-2.99	-1.66
P3	0	-8.18	-8.18	-33.47	-85.6	-55.66	-3.14	-3.11	-1.66
P2	0	-8.09	-8.09	-33.55	-81.41	-57.54	-3.48	-2.69	-1.8
P2	0	-8.01	-8.01	-42.24	-87.56	-66.8	-2.67	-3.3	-1.84
P5	0	-7.99	-7.99	-39.78	-79.32	-60.21	-2.89	-3.18	-1.53
P4	0	-7.96	-7.96	-36.76	-86.89	-56.61	-3.45	-3.01	-1.49
P3	0	-7.85	-7.85	-37.29	-90.56	-62.6	-2.67	-3.31	-1.9
P4	0	-7.8	-7.8	-37.68	-83.45	-61.84	-3.34	-2.66	-1.81
P5	0	-7.74	-9.11	-36.46	-81.27	-61.49	-4.31	-3.11	-1.88
P16	-1	-7.52	-7.66	-31.05	-69.52	-52.88	-1.18	-2.69	-1.64
P10	0	-7.46	-7.46	-42.94	-81.64	-59.95	-2.84	-3.18	-1.28
P6	0	-7.33	-7.33	-39.29	-76.23	-59.53	-2.23	-3.36	-1.52
P16	0	-7.33	-7.33	-31.27	-67.82	-53.67	-2.48	-2.79	-1.68
P2	0	-7.31	-7.31	-40.65	-82.19	-60.99	-2.6	-3.13	-1.53
P2	0	-7.28	-7.28	-41.57	-83.63	-59.78	-2.18	-3.35	-1.37
P5	-1	-7.22	-7.69	-39.88	-76.57	-66.96	-2.15	-3.6	-2
P3	-1	-7.22	-7.69	-40.88	-72.24	-64.02	-1.97	-3.72	-1.74
P21	0	-7.22	-7.22	-36.75	-77.19	-57.22	-2.16	-3.09	-1.54
P4	0	-7.16	-7.16	-38.7	-81.28	-58.13	-2.58	-2.93	-1.46
P5	-1	-7.16	-7.63	-24.11	-77.06	-53.02	-3.21	-2.12	-2
P20	0	-7.11	-7.11	-40.14	-74.1	-57.77	-2.71	-2.97	-1.32
P6	-1	-7.07	-7.54	-32.54	-74.74	-57.67	-3.02	-2.51	-1.88
P11	0	-7	-7	-39.28	-70.24	-56.9	-2.67	-2.87	-1.32
P16	0	-6.98	-6.98	-33	-65.68	-53.25	-2.69	-2.59	-1.52
P3	0	-6.96	-8.31	-39.76	-87.27	-64.24	-3.4	-3.13	-1.84
P21	0	-6.95	-6.95	-39.1	-69.25	-57.63	-2.23	-3.44	-1.39
P5	-1	-6.89	-7.36	-32.11	-68.86	-56.81	-0.57	-3.45	-3.35
P1	0	-6.88	-6.88	-38.81	-81.28	-59.35	-2.59	-2.9	-1.54
P1	0	-6.86	-6.86	-40.36	-81.32	-58.89	-2.37	-3.23	-1.39
P16	0	-6.81	-6.81	-39.5	-68.08	-59.34	-2.22	-3.15	-1.49
P1	0	-6.81	-6.81	-36.84	-77.01	-55.75	-2.66	-2.68	-1.42
P3	-1	-6.8	-7.27	-26.62	-81.3	-54.86	-2.89	-2.15	-2
P20	0	-6.79	-6.79	-40.01	-69.32	-56.11	-1.82	-3.53	-1.21
P2	-1	-6.77	-7.24	-38.82	-70.8	-64.54	-2.38	-2.94	-1.93

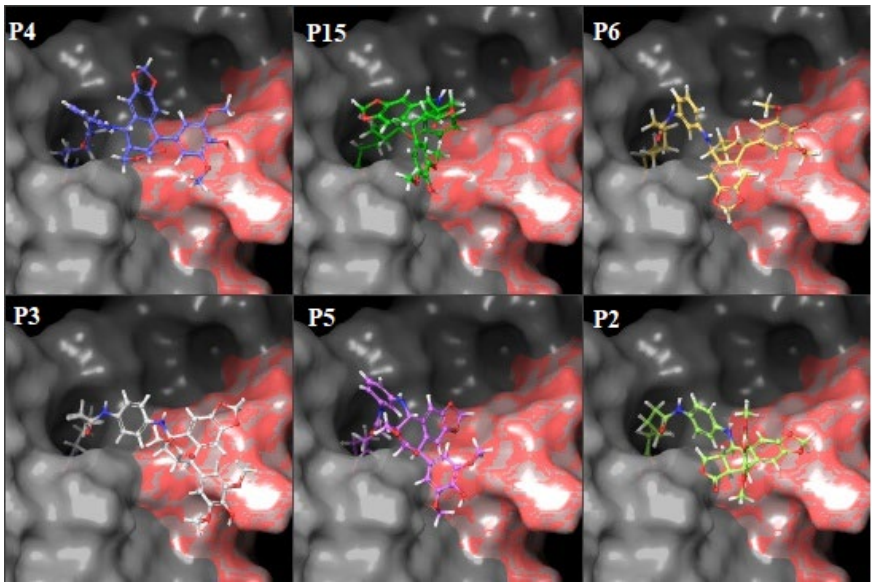


Fig. S7 PPT cap group of some top–scoring poses (P4, P15, P6, P3, P5 and P2) interacting with HDAC6 protein surface defined by loop L1 (colored pink)

Table S9 QikProp descriptors of C1-C8, P1-P21 and their components drugs

ID	#stars	#rotor	#rtvFG	MW	SASA	FOSA	FISA	PISA	Vol
SAHA	0	9	1	264.32	594.36	207.15	179.25	207.96	975.33
CPT	0	2	0	348.3	576.06	191.06	143.24	241.76	1026.91
Etoposide	0	7	4	588.56	727.89	515.01	130.75	82.14	1479.69
C1	5	11	1	574.59	931.54	421.28	321.99	188.27	1693.53
C2	4	12	1	588.62	964.16	453.78	321.93	188.45	1753.92
C3	5	13	1	602.65	997.40	487.09	321.95	188.36	1814.69
C4	5	14	1	616.67	1030.42	520.07	321.94	188.41	1875.29
C5	7	15	1	630.70	1063.45	553.05	321.99	188.41	1935.88
C6	4	11	1	560.56	925.22	369.98	322.43	232.81	1659.26
C7	5	12	1	574.59	958.46	403.28	322.46	232.72	1720.03
C8	4	13	1	588.62	991.42	436.20	322.45	232.77	1780.59
P1	5	12	3	633.65	934.80	443.64	260.86	230.30	1777.31
P2	7	13	3	647.68	969.15	477.12	260.74	231.29	1838.43
P3	7	14	3	661.71	1000.90	509.69	260.88	230.32	1898.49
P4	5	12	3	633.65	930.58	438.09	255.35	237.15	1774.87
P5	6	13	3	647.68	953.07	458.59	258.57	235.91	1831.99
P6	6	14	3	661.71	991.57	496.00	260.01	235.55	1886.42
P7	1	11	3	592.60	860.29	413.11	213.71	233.46	1638.64
P8	1	12	3	606.63	881.49	449.61	222.28	209.61	1690.64
P9	2	13	3	620.65	918.98	467.56	224.79	226.63	1760.35
P10	2	14	3	634.68	959.16	511.93	213.76	233.46	1820.35
P11	3	15	3	648.71	992.14	544.93	213.73	233.49	1880.91
P12	1	11	3	592.60	851.91	395.93	213.56	242.43	1632.25

P13	1	12	3	606.62	844.84	421.98	211.44	211.42	1665.54
P14	1	13	3	620.65	716.54	348.83	137.09	230.61	1564.75
P15	2	14	3	634.68	946.81	486.71	220.13	239.96	1803.52
P16	2	15	3	648.71	941.71	487.55	215.30	238.85	1845.15
P17	1	11	3	592.60	858.91	409.39	211.35	238.18	1639.78
P18	2	12	3	606.63	891.79	442.20	211.41	238.19	1700.27
P19	2	13	3	620.65	873.18	448.67	221.13	203.39	1714.87
P20	2	14	3	634.68	913.05	476.97	223.24	212.84	1786.95
P21	2	15	3	648.71	938.48	514.99	221.03	202.46	1836.08

Table S9 (contd.) QikProp descriptors of C1-C8, P1-P21 and their components drugs

ID	Donor HB	Accpt HB	logP_{C16}	logP_{oct}	logP_{w}	log$P_{o/w}$	log$S$	logHERG	P_{Caco}
SAHA	3	6.7	10.56	17.29	15.28	0.739	-2.14	-4.38	106.86
CPT	1	7.75	10.72	18.49	12.38	1.742	-3.69	-5.04	434.03
Etoposide	3	16.95	13.98	29.96	22.46	0.606	-2.82	-4.14	570.21
C1	3	15.2	18.74	33.47	24.87	0.662	-4.62	-5.30	4.72
C2	3	15.2	19.40	32.88	24.70	1.014	-4.99	-5.43	4.76
C3	3	15.2	20.09	34.47	24.58	1.37	-5.36	-5.56	4.73
C4	3	15.2	20.77	33.96	24.43	1.728	-5.75	-5.69	4.74
C5	3	15.2	21.46	36.29	24.28	2.087	-6.13	-5.81	4.75
C6	3	15.2	18.79	32.13	25.13	0.496	-4.54	-5.59	4.71
C7	3	15.2	19.47	34.47	25.01	0.848	-4.90	-5.73	4.68
C8	3	15.2	20.15	33.22	24.84	1.203	-5.28	-5.85	4.71
P1	5	14.45	19.57	35.35	26.70	1.726	-4.75	-5.15	17.99
P2	5	14.45	20.24	37.15	26.58	2.072	-5.11	-5.32	17.99
P3	5	14.45	20.88	36.68	26.42	2.415	-5.45	-5.45	17.99
P4	5	14.45	19.53	35.49	26.69	1.763	-4.69	-5.14	20.36
P5	5	14.45	20.07	37.24	26.53	2.075	-4.87	-5.17	18.99
P6	5	14.45	20.75	36.42	26.41	2.362	-5.31	-5.41	18.42
P7	4	12.7	17.59	31.31	23.26	2.08	-4.31	-4.81	50.29
P8	4	12.7	17.96	32.70	22.90	2.3	-4.52	-4.74	42.64
P9	4	12.7	18.83	32.42	22.97	2.705	-4.92	-5.01	39.69
P10	4	12.7	19.50	33.36	22.81	3.13	-5.40	-5.29	50.54
P11	4	12.7	20.16	33.51	22.68	3.486	-5.77	-5.43	50.53
P12	4	12.7	17.55	31.49	23.30	2.062	-4.18	-4.76	50.45
P13	4	12.7	17.49	31.99	22.85	2.269	-3.91	-4.33	52.75
P14	4	12.7	15.95	30.87	22.12	2.387	-1.77	-2.72	255.85
P15	4	12.7	19.38	32.87	22.89	2.999	-5.19	-5.24	43.78
P16	4	12.7	19.53	33.85	22.63	3.309	-4.94	-4.98	48.52
P17	4	12.7	17.60	31.98	23.27	2.111	-4.29	-4.80	52.99
P18	4	12.7	18.23	32.06	23.1	2.457	-4.65	-4.97	53.32
P19	4	12.7	18.00	32.56	22.68	2.471	-4.19	-4.47	42.96
P20	4	12.7	18.82	33.16	22.63	2.881	-4.66	-4.73	41.10
P21	4	12.7	19.23	33.62	22.39	3.172	-4.90	-4.80	43.05

Table S9 (contd.) QikProp descriptors of C1-C8, P1-P21 and their components drugs

ID	logBB	P_{MDCK}	#metab	logK_{hsa}	PSA	#NandO	ROF	#ring atm	#nonH atm
SAHA	-1.84	85.80	3	-0.75	102.24	5	0	6	19
CPT	-0.86	200.7	3	-0.16	97.92	6	0	21	26
Etoposide	-1.03	269.56	8	-0.72	159.85	13	2	32	42
C1	-4.04	2.95	7	-0.65	203.34	13	2	26	42
C2	-4.19	2.96	7	-0.56	203.37	13	2	26	43
C3	-4.34	2.96	7	-0.46	203.35	13	2	26	44
C4	-4.49	2.96	7	-0.37	203.37	13	2	26	45
C5	-4.64	2.95	7	-0.27	203.37	13	2	26	46
C6	-4.10	2.92	6	-0.74	203.53	13	2	26	41
C7	-4.26	2.92	6	-0.65	203.51	13	2	26	42
C8	-4.41	2.92	6	-0.55	203.54	13	2	26	43
P1	-3.18	12.50	9	-0.34	203.53	13	2	28	46
P2	-3.32	12.54	9	-0.26	203.47	13	2	28	47
P3	-3.45	12.49	9	-0.18	203.55	13	2	28	48
P4	-3.09	14.24	11	-0.34	203.49	13	2	28	46
P5	-3.21	13.20	11	-0.26	203.70	13	2	28	47
P6	-3.41	12.75	11	-0.20	202.63	13	2	28	48
P7	-2.43	38.04	10	-0.27	174.71	12	2	28	43
P8	-2.60	31.08	10	-0.19	175.23	12	2	28	44
P9	-2.77	29.28	9	-0.08	176.34	12	2	28	45
P10	-2.80	37.99	10	0.00	174.73	12	2	28	46
P11	-2.92	38.03	10	0.09	174.73	12	2	28	47
P12	-2.40	38.18	10	-0.28	174.68	12	2	28	43
P13	-2.34	40.13	10	-0.21	175.86	12	2	28	44
P14	-1.32	232.05	10	-0.31	165.99	12	2	28	45
P15	-2.84	32.69	10	-0.04	173.90	12	2	28	46
P16	-2.74	36.64	10	0.05	175.18	12	2	28	47
P17	-2.40	40.22	11	-0.26	173.22	12	2	28	43
P18	-2.52	40.17	10	-0.18	173.25	12	2	28	44
P19	-2.56	31.93	10	-0.15	172.19	12	2	28	45
P20	-2.73	30.38	10	-0.04	172.56	12	2	28	46
P21	-2.81	32.01	10	0.03	172.27	12	2	28	47