

Prediction of Tumour Tissue Diffusion Coefficients of Hypoxia-Activated Prodrugs from Physicochemical Parameters

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Table S1. Structures, physicochemical parameters, calculated D_{mcl} (from Eq. 1 using the coefficients for HT29 in Study A as listed in Table 1) and measured D_{mcl} for HT29 MCLs. Errors are SEM and units of D_{mcl} are cm^2s^{-1} . The calculated D_{mcl} values were based on measured $\log P_{7.4}$ when available.

SN	Ref ^a	Structure	MW ^b	HD ^c	HA ^d	Calculated $\log P_{7.4}$	Measured $\log P_{7.4}$	Calculated $D_{mcl} \times 10^6$	Measured $D_{mcl} \times 10^6$	
									Study A	Study B
24280 (TPZ)			178	2	6	0.33 ± 0.02	-0.38 ± 0.05	0.417	0.404 ± 0.013	
26434	1		162	2	5	1.06 ± 0.22	1.06 ± 0.06	1.80	3.04 ± 0.10	
26955	2		455	2	8	1.69 ± 0.31	1.69 ± 0.10	0.691	0.617 ± 0.125	
27140	3		470	2	10	1.84 ± 0.2	1.84 ± 0.03	0.426	0.541 ± 0.008	

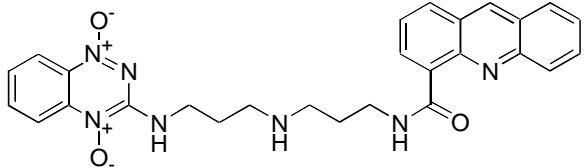

27149	3		498	3	10	0.88±0.4	0.88±0.03	0.150	0.152 ± 0.0074	
27758	4		192	2	6	0.14±0.21	0.127±0.003	0.579	0.662 ± 0.022	

Table S1, continued (page 2)

SN	Ref ^a	Structure	MW	HD	HA	Calculated logP _{7.4}	Measured logP _{7.4}	Calculated $D_{mcl} \times 10^6$	Measured $D_{mcl} \times 10^6$	
									Study A	Study B
27759	4		192	2	6	0.08±0.20	0.068±0.025	0.553	0.543 ± 0.025	
27769	4		192	2	6	0.24±0.20	0.241±0.034	0.632	0.750 ± 0.018	
27791	4		213	2	6	0.44±0.18	0.441±0.009	0.699	0.870 ± 0.022	
27800	4		213	2	6	0.17±0.18	0.166±0.005	0.560	0.669 ± 0.024	
27820	4		256	2	8	-1.15±0.25	-1.15±0.05	0.219	0.213 ± 0.031	
27849	4		246	2	6	0.81±0.24	0.815±0.046	0.876	0.793 ± 0.054	
27866	4		256	2	8	-1.38±0.23	-1.38±0.02	0.213	0.319 ± 0.034	

Table S1, continued (page 3)

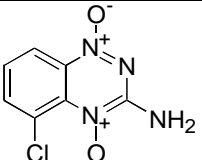
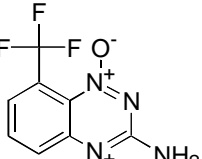
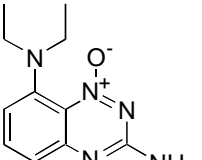
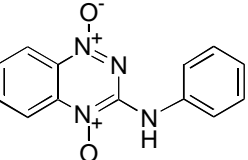
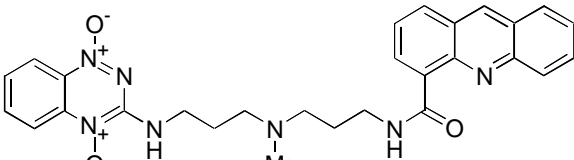
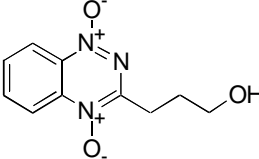
SN	Ref ^a	Structure	MW	HD	HA	Calculated logP _{7.4}	Measured logP _{7.4}	Calculated <i>D</i> _{mcl} × 10 ⁶	Measured <i>D</i> _{mcl} × 10 ⁶	
									Study A	Study B
27891	4		213	2	6	-0.1±0.2	-0.10±0.03	0.460	0.354 ± 0.006	
27916	4		246	2	6	0.48±0.24	0.479±0.038	0.659	0.515 ± 0.012	
28019	4		249	2	7	0.83±0.18	0.83±0.01	0.654	0.453 ± 0.018	
28098	5		254	1	6	1.51±0.17	1.43±0.01	2.265	2.700 ± 0.058	
28141	3		512	2	10	1.53±0.27	1.53±0.04	0.315	0.382 ± 0.004	
28246	6		221	1	6	-0.47±0.25	-0.47 ^f	0.807	0.494 ± 0.018	

Table S1, continued (page 4)

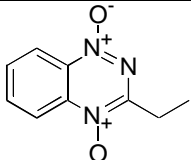
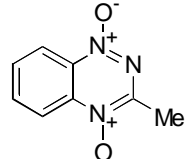
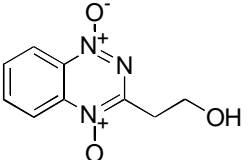
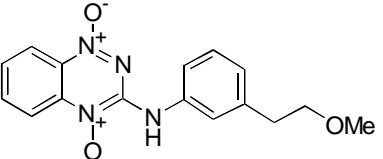
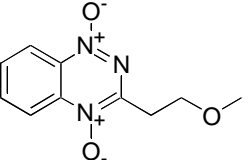
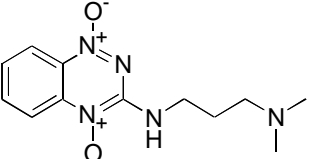
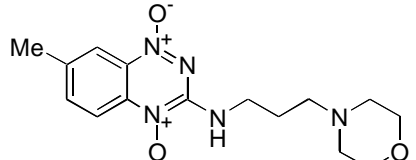
SN	Ref ^a	Structure	MW	HD	HA	Calculated logP _{7.4}	Measured logP _{7.4}	Calculated <i>D</i> _{mcl} × 10 ⁶	Measured <i>D</i> _{mcl} × 10 ⁶	
									Study A	Study B
28266	7		191	0	5	0.34±0.21	0.22±0.06	2.86	2.610 ± 0.011	
28287	7		177	0	5	-0.21±0.20	-0.22 ^f	2.69	1.920 ± 0.280	
28293	6		207	1	6	-0.91±0.14		0.584	0.441 ± 0.054	
28361	5		312	1	7	1.51±0.19	1.51±0.024	1.84	2.400 ± 0.001	
28400	7		221	0	6	-0.26±0.22	0.187±0.027	2.09	2.090 ± 0.036	
28402	8		263	1	7	-2.01±0.38	-2.01±0.07	0.240	0.187 ± 0.012	
28425	np ^e		319	1	8	0.22±0.20	0.223±0.009	0.638	0.770 ± 0.087	

Table S1, continued (page 5)

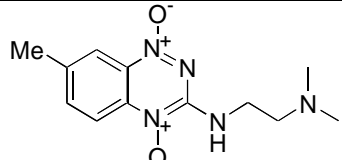
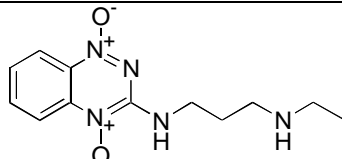
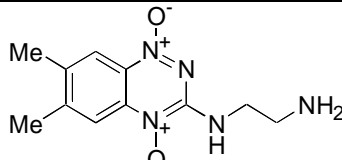
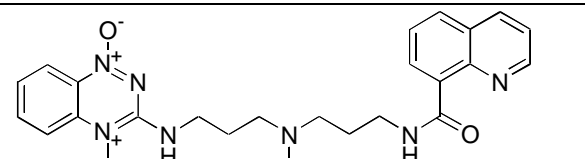
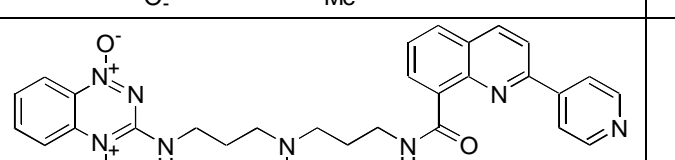
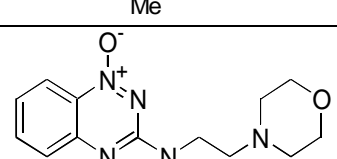
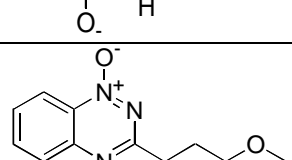
SN	Ref ^a	Structure	MW	HD	HA	Calculated logP _{7.4}	Measured logP _{7.4}	Calculated $D_{mcl} \times 10^6$	Measured $D_{mcl} \times 10^6$	
									Study A	Study B
28427	9		263	1	7	-0.78±0.25	-0.74±0.05	0.438	0.509 ± 0.028	
28433	np		263	2	7	-2.62±0.45	-2.62±0.02	0.1996	0.139 ± 0.001	
28436	np		249	3	7	-1.48±0.24	-1.48±0.02	0.207	0.325 ± 0.021	
28565	3		462	2	10	0.29 ± 0.03	0.148 ± 0.004	0.1693	0.128 ± 0.041	
28588	3		539	2	11	0.66±0.34	0.665±0.023	0.161	0.976 ± 0.046	
28606	8		291	1	8	-0.37±0.18	-0.35±0.04	0.424	0.363 ± 0.004	
28614	6		235	0	6	-0.02±0.27		2.143	2.13 ± 0.174	

Table S1, continued (page 6)

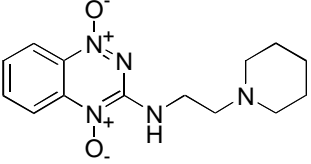
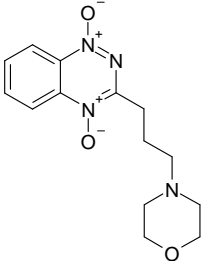
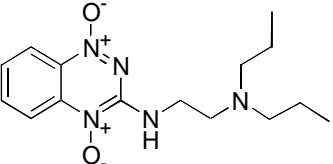
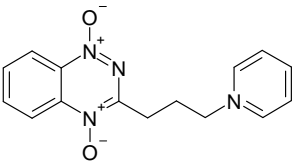
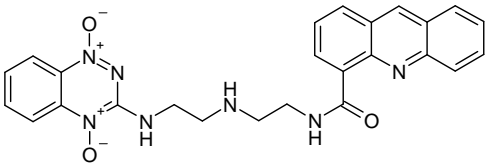
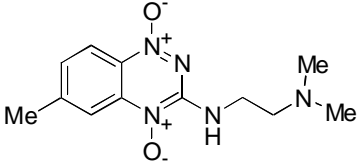
SN	Ref ^a	Structure	MW	HD	HA	Calculated logP _{7.4}	Measured logP _{7.4}	Calculated $D_{mcl} \times 10^6$	Measured $D_{mcl} \times 10^6$	
									Study A	Study B
28620	8		289	1	7	-0.46±0.25	0.471±0.011	0.509	0.723 ± 0.045	
28627	8		290	0	7	-1.86±0.59		0.410	0.747 ± 0.064	
28643	8		305	1	7	0.49±0.29	0.488±0.066	1.082	1.71 ± 0.226	
28648	6		288	0	6	-1.27±0.32	-1.27±0.03	0.887	0.650 ± 0.010	
28660	3		470	3	10	1.36±0.24	1.36±0.04	0.172	0.192 ± 0.016	
28682	8		263	1	7	-0.77±0.25	-0.71±0.04	0.448	0.399 ± 0.013	0.211

Table S1, continued (page 7)

SN	Ref ^a	Structure	MW	HD	HA	Calculated logP _{7.4}	Measured logP _{7.4}	Calculated $D_{mcl} \times 10^6$	Measured $D_{mcl} \times 10^6$	
									Study A	Study B
28713	np		497	1	9	1.88±0.59		1.21	1.470 ± 0.006	
28823***	6		279	1	8	-0.85±0.26	0.854±0.015	0.315	0.232 ± 0.008	
28852	6		317	1	7	-0.21±0.24		0.597	0.681 ± 0.051	
28860	3		484	2	10	3	2.15±0.02	0.545	0.399 ± 0.034	
28864	6		303	1	7	6	0.001±0.012	0.735	0.749 ± 0.071	
28870	np		250	1	7	np	0.356±0.057	1.11	1.320 ± 0.108	0.803
28871	np		553	2	11	np		0.188	0.225 ± 0.035	

Table S1, continued (page 8)

SN	Ref ^a	Structure	MW	HD	HA	Calculated logP _{7.4}	Measured logP _{7.4}	Calculated $D_{mcl} \times 10^6$	Measured $D_{mcl} \times 10^6$	
									Study A	Study B
28874	np		498	2	10	np		0.776	0.734 ± 0.183	
28875	np		236	2	7	np		0.363	0.248 ± 0.004	
28890	8		331	1	7	0.25±0.34	0.252±0.007	0.856	0.945 ± 0.059	
29039	np		235	0	6	0.20±0.22		2.30	1.740 ± 0.114	
29047	7		177	0	5	1.09±0.25		3.39	3.80 ± 0.24	
29051	8		233	1	6	0.39±0.24		1.52	1.83 ± 0.31	
29053	10		219	2	6	-0.83±0.28		0.307	0.519 ± 0.015	
29102	8		305	1	7	0.65±0.26	0.655±0.025	1.22	0.863 ± 0.035	0.811

Table S1, continued (page 9)

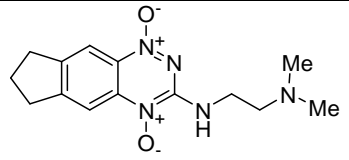
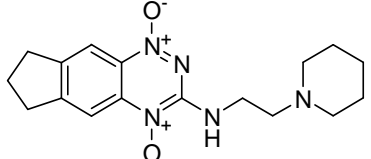
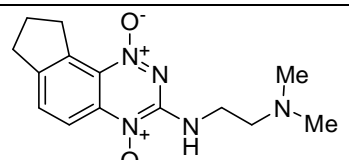
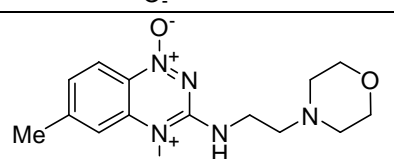
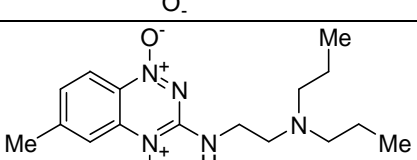
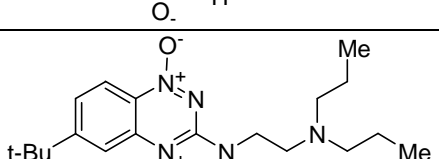
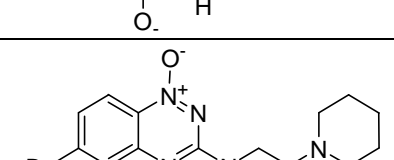
SN	Ref ^a	Structure	MW	HD	HA	Calculated logP _{7.4}	Measured logP _{7.4}	Calculated $D_{mcl} \times 10^6$	Measured $D_{mcl} \times 10^6$	
									Study A	Study B
29143	11		289	1	7	-0.07±0.26	-0.071 ±0.021	0.712	0.590 ± 0.033	
29146	11		329	1	7	0.62±0.27	0.619±0.007	1.13	1.19 ± 0.05	
29147	11		289	1	7	0.18±0.26	0.179±0.020	0.878	0.835 ± 0.046	
29267	8		305	1	8	0.07±0.20	0.072±0.024	0.577	0.452 ± 0.006	
29270	8		319	1	7	0.95±0.30		1.42	1.48 ± 0.07	
29273	8		361	1	7	2.63±0.27		2.09	1.75 ± 0.11	
29347	8		345	1	7	1.23±0.27		1.55	1.50 ± 0.07	0.975

Table S1, continued (page 10)

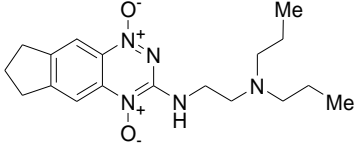
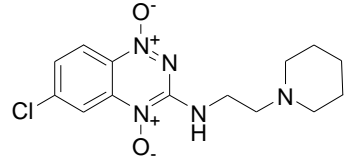
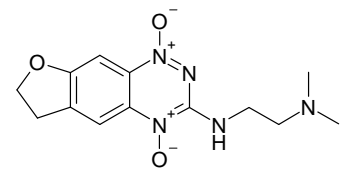
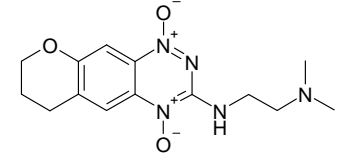
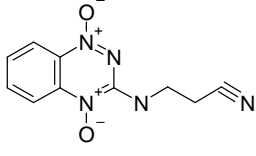
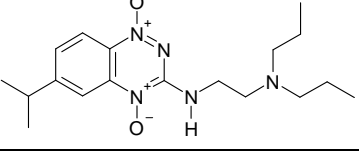
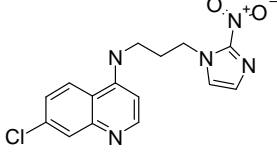
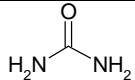
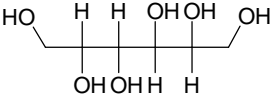
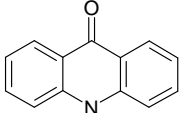
SN	Ref ^a	Structure	MW	HD	HA	Calculated logP _{7.4}	Measured logP _{7.4}	Calculated $D_{mcl} \times 10^6$	Measured $D_{mcl} \times 10^6$	
									Study A	Study B
29375	11		345	1	7	1.61±0.30		1.79	1.93 ± 0.14	
29390	8		324	1	7	0.44±0.49		1.01	1.10 ± 0.08	
29650***	11		291	1	8	-1.05±0.25	-1.05±0.01	0.279	0.427 ± 0.007	
29662***	11		305	1	8	-0.54±0.26	-0.54±0.01	0.360	0.454 ± 0.061	
28205	np		231	1	7	-0.53±0.45		0.409	0.503± 0.049	0.260
29366	np		348	1	7	1.82±0.48		1.47	2.17 ± 0.17	
NLCQ-1	12		332	1	7	0.22	0.22 ⁹	0.834	0.606 ± 0.003	

Table S1, continued (page 11)

SN	Ref ^a	Structure	MW	HD	HA	Calculated logP _{7.4}	Measured logP _{7.4}	Calculated $D_{mcl} \times 10^6$	Measured $D_{mcl} \times 10^6$	
									Study A	Study B
Urea			60.1	4	3	-2.01±0.22	-2.01±0.05	0.498	0.450 ± 0.023	0.450
Mannitol			182	6	6	-2.62±0.28	-2.62±0.04	0.245	0.211 ± 0.0002	0.182
Acridan-9(10H)one			195	1	2	2.96±0.25	2.96±0.10	3.29	3.17 ± 0.007	3.52

*** in table but not in graph

Footnotes:^a References to synthesis and characterisation

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^b Molecular Weight (daltons)

^c Number of hydrogen bond donors

^d Number of hydrogen bond acceptors

^e np, not published

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^gRef 12 above