Correlation plot of experimentally determined *n*-octanol/water partition coefficient (Log*P*) and predicted (cLog*P*)

Experimentally determined Log*P* were plotted against cLog*P* values for 35 drugs. The dotted lines represent the boundaries of the 95% CI and R^2 represents the goodness of fit. Correlation is shown in **Supplementary Figure 1**.

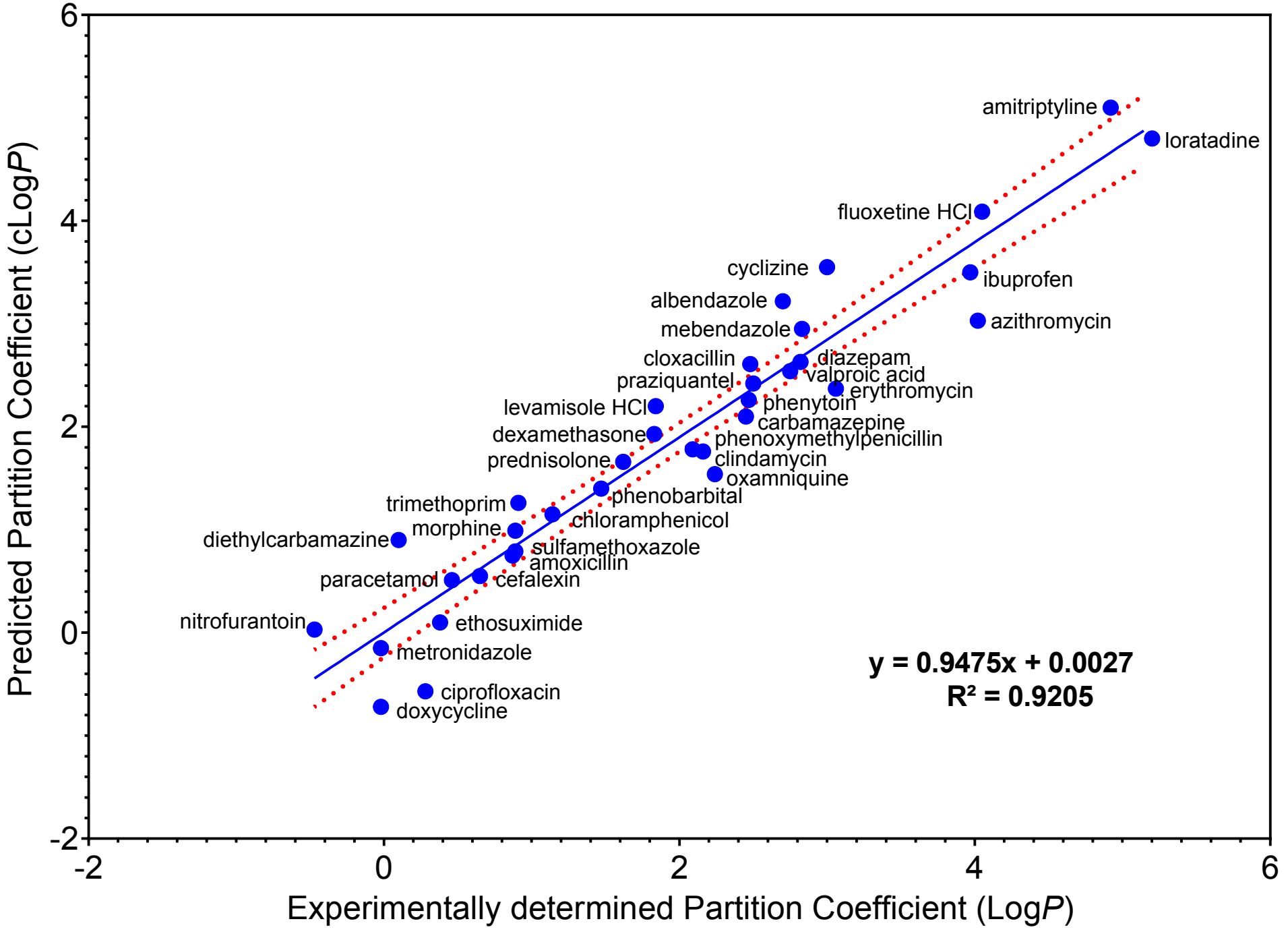
Benchmark Reference Drug Molecule

Metoprolol was used in previous studies as a benchmark reference compound for permeability because it is known that 95% of the drug is absorbed from the GI tract mainly by passive diffusion (1, 2). Similarly in this study, metoprolol was chosen as the benchmark reference compound for high/low permeability. Drugs with cLog*P* values similar or above the cLog*P* value of metoprolol (1.8) were classified as high permeability class drugs, whereas, drugs with cLog*P* values less than that of metoprolol were classified as low permeability class drugs. Permeability classification is presented in **Supplementary Table 1**.

Supplementary Table 1: Permeability classification of the 38 drugs used in the study

Drug	**cLog*P***	**Permeability class**
Albendazole	3.22	High
Amitriptyline	5.1	High
Amoxicillin	0.75	Low
Azithromycin	3.03	High
Carbamazepine	2.1	High
Cefalexin	0.55	Low
Chloramphenicol	1.15	Low
Ciprofloxacin	-0.57	Low
Clindamycin	1.76	Low
Cloxacillin	2.61	High
Cyclizine	3.55	High
Dexamethasone	1.93	High
Diazepam	2.63	High
Diethylcarbamazine	0.9	Low
Doxycycline	-0.72	Low
Erythromycin	2.37	High
Ethosuximide	0.1	Low
Fluoxetine HCl	4.09	High
Ibuprofen	3.5	High
Ivermectin	5.83	High
Levamisole HCl	2.2	High
Loratadine	4.8	High
Mebendazole	2.95	High
Metronidazole	-0.15	Low
Midazolam	3.89	High

Drug	**cLog*P***	**Permeability class**
Morphine	0.99	Low
Niclosamide	4.49	High
Nitrofurantoin	0.03	Low
Oxamniquine	1.54	Low
Paracetamol	0.51	Low
Phenobarbital	1.4	Low
Phenoxymethylpenicillin	1.78	Low
Phenytoin	2.26	High
Praziquantel	2.42	High
Prednisolone	1.66	Low
Sulfamethoxazole	0.79	Low
Trimethoprim	1.26	Low
Valproic acid	2.54	High



Supplementary Figure 1: Correlation plot of experimentally determined n-octanol/water partition coefficient (LogP) and predicted (cLogP) values for 35 drugs. The dotted lines represent the boundaries of the 95% CI and R^2 represents the goodness of fit.

Solubility percent change to cause a shift in the solubility class

Taking a conservative approach in using the BCS-based biowaiver principles, more risk is considered when the solubility class of a drug shifts from high to low than *vice versa*. According to the BCS principles, drugs with a dose number (D_0) ≤ 1 are classified as high solubility class drugs and, conversely, drugs with a $D_0 > 1$ are classified as low solubility class drugs. The D_0 is a function of the drug's maximal dose strength (M_0), saturated solubility (C_s) and initial gastric volume (V_0). To account for possible discrepancies in solubility of drugs in pediatric subpopulations, percentages above which experimental solubility used in this study might change to cause a shift in the solubility class from high to low (i.e. to bring the D_0 of a drug above 1) were calculated using supplementary equation 1.

$$\%\ change\ in\ solubility = 1 - D_0 \qquad (Supplementary\ equation\ 1)$$

Supplementary Table 2 displays percent changes (reduction) in solubility above which a shift in the solubility class from high to low in pediatric subpopulations would be expected. For example, when the experimental solubility of amoxicillin would decrease by more than 5%, the low solubility class designated in 12 years child would shift from high to low.

Supplementary Table 2: Solubility percent change above which a shift in the solubility class for high solubility drugs in pediatric subpopulations would be expected

	Percent change																		
		Age (years)																	
Drug	**Newborn (neonate)**	**0.5**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**
Amoxicillin	The drug shows low solubility													0.05	0.15	0.24	0.31	0.37	0.41
Cefalexin	The drug shows low solubility						0.0009	The drug shows low solubility						0.09	0.19	0.27	0.34	0.39	0.43
Chloramphenicol	The drug shows low solubility										0.09	0.17	0.26	0.35	0.42	0.48	0.53	0.57	0.59
Ciprofloxacin	0.87	0.82	0.79	0.83	0.85	0.86	0.88	0.89	0.90	0.92	0.92	0.93	0.94	0.95	0.95	0.96	0.96	0.96	0.97
Cyclizine	0.74	0.74	0.74	0.74	0.74	0.74	0.74	0.74	0.74	0.75	0.77	0.79	0.82	0.67	0.71	0.74	0.76	0.78	0.80
Dexamethasone	0.01	0.25	0.42	0.53	0.58	0.63	0.68	0.72	0.74	0.77	0.79	0.81	0.83	0.85	0.87	0.88	0.89	0.90	0.91
Diazepam	The drug shows low solubility										0.09	0.17	0.26	The drug shows low solubility			0.05	0.13	0.18
Diethylcarbamazine	0.89	0.95	0.96	0.97	0.97	0.97	0.98	0.98	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
Ethosuximide	0.86	0.86	0.84	0.87	0.88	0.89	0.91	0.92	0.93	0.93	0.94	0.95	0.95	0.96	0.96	0.97	0.97	0.97	0.97

	Percent change																		
		Age (years)																	
Drug	**Newborn (neonate)**	**0.5**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**
Fluoxetine HCl	The drug shows low solubility										0.996	0.997	0.997	0.997	0.998	0.998	0.998	0.998	0.998
Levamisole HCl	0.952	0.976	0.982	0.985	0.987	0.988	0.990	0.991	0.992	0.993	0.993	0.994	0.995	0.995	0.996	0.996	0.997	0.997	0.997
Metronidazole	0.79	0.79	0.79	0.12	0.22	0.30	0.40	0.47	0.51	0.57	0.62	0.65	0.69	0.72	0.75	0.78	0.80	0.82	0.83
Morphine	0.82	0.64	0.64	0.64	0.64	0.64	0.64	0.64	0.64	0.64	0.64	0.44	0.51	0.56	0.61	0.65	0.68	0.71	0.73
Paracetamol	0.42	0.71	0.78	0.73	0.76	0.79	0.75	0.78	0.79	0.82	0.67	0.70	0.74	0.77	0.79	0.81	0.83	0.84	0.85
Phenobarbital	The drug shows low solubility									0.08	0.18	0.25	0.34	0.41	0.48	0.53	0.57	0.61	0.63
Phenoxymethylpenicillin	0.58	0.79	0.68	0.74	0.77	0.79	0.82	0.84	0.71	0.75	0.77	0.79	0.82	0.84	0.85	0.87	0.88	0.89	0.90
Prednisolone	The drug shows low solubility											0.07	0.17	0.27	0.35	0.42	0.47	0.51	0.54
Trimethoprim	The drug shows low solubility																0.05	0.13	0.18

REFERENCES

1. Shawahna R, Rahman N. Evaluation of the use of partition coefficients and molecular surface properties as predictors of drug absorption: a provisional biopharmaceutical classification of the list of national essential medicines of Pakistan. Daru. 2011;19(2):83-99.
2. Kasim NA, Whitehouse M, Ramachandran C, Bermejo M, Lennernäs H, Hussain AS, et al. Molecular properties of WHO essential drugs and provisional biopharmaceutical classification. Mol Pharm. 2004;1(1):85-96.