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Research Article

BDDCS Applied to Over 900 Drugs

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Abstract. Here, we compile the Biopharmaceutics Drug Disposition Classification System (BDDCS) classification for 927 drugs, which include 30 active metabolites. Of the 897 parent drugs, 78.8% (707) are administered orally. Where the lowest measured solubility is found, this value is reported for 72.7% (513) of these orally administered drugs and a dose number is recorded. The measured values are reported for percent excreted unchanged in urine, Log*P*, and Log$D_{7.4}$ when available. For all 927 compounds, the *in silico* parameters for predicted Log solubility in water, calculated Log*P*, polar surface area, and the number of hydrogen bond acceptors and hydrogen bond donors for the active moiety are also provided, thereby allowing comparison analyses for both *in silico* and experimentally measured values. We discuss the potential use of BDDCS to estimate the disposition characteristics of novel chemicals (new molecular entities) in the early stages of drug discovery and development. Transporter effects in the intestine and the liver are not clinically relevant for BDDCS class 1 drugs, but potentially can have a high impact for class 2 (efflux in the gut, and efflux and uptake in the liver) and class 3 (uptake and efflux in both gut and liver) drugs. A combination of high dose and low solubility is likely to cause BDDCS class 4 to be underpopulated in terms of approved drugs (N=53 compared with over 200 each in classes 1–3). The influence of several measured and *in silico* parameters in the process of BDDCS category assignment is discussed in detail.

KEY WORDS: BDDCS; biowaiver; dose number; extent of metabolism; permeability rate.

In 2005, Wu and Benet (1) introduced the Biopharmaceutics Drug Disposition Classification System (BDDCS). Wu and Benet recognized that there was a very strong correlation between the intestinal permeability rate and the extent of metabolism. For example, Benet *et al.* (2) noted that for the 29 drugs and endogenous substances for which human jejunal permeability rate measurements were available, there was an excellent correlation between these permeability rate measurements and the extent of drug metabolism in humans. Fourteen of the 16 drugs exhibiting human intestinal permeability rates greater than metoprolol were extensively metabolized, while 11 of 12 drugs showing permeability rates less than metoprolol were poorly metabolized. Two drugs showing disparity between the permeability rate and metabolism, cephalexin and losartan, exhibit permeability rates that differ by no more than 16% from metoprolol (2). Since the coefficients of variation for the human permeability parameters range from 29% to 130%, these borderline compounds may in fact also have followed the correlation. The correlation between the extent of metabolism and human intestinal jejunal permeability was markedly better than that observed for intestinal jejunal permeability and partition coefficient by Takagi *et al.* (3), who noted that Log *P* measured and calculated correctly predict high *versus* low permeability only about two thirds of the time. Wu and Benet (1) reasoned that it might be easier to utilize metabolism in assigning drug classification since it is difficult and expensive to determine human intestinal permeabilities and since it is also difficult to obtain quantitative mass balance measures that show ≥90% absorption, the FDA criterion for a biowaiver as defined in the FDA BCS Guidance (4), based on the work of Amidon *et al.* (5). Therefore, in proposing the BDDCS classification system, Wu and Benet (1) substituted extensive and poor metabolism for high and low permeability in the BCS while utilizing the same criteria as the FDA for high and low solubility. That is, a high solubility compound at the highest marketed dose strength would be soluble in 250 mL of water over the pH range of 1–7.5 at 37°C. Using the BDDCS, Wu and Benet (1) classified 168 drugs based on the extent of metabolism and solubility.

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BDDCS *VERSUS* BCS

Although BDDCS grew out of the FDA's BCS Guidance (4), Wu and Benet (1) proposed BDDCS as a means to predict the drug disposition characteristics of novel chemicals (here, referred to as "new molecular entities", NMEs) during the early stages of drug discovery and development. Such examples will be discussed below. Recently, Benet and Larregieu (6) reviewed the differences between BCS and BDDCS in terms of purpose and basis. The purpose of BCS is to facilitate biowaivers of *in vivo* bioequivalence studies for drugs that exhibit no significant intestinal absorption problems. In contrast, the purpose of BDDCS is to predict the drug disposition of NMEs as well as potential drug–drug interactions for NMEs and drugs on the market with respect to the intestine and liver. Very recently, a consensus paper with respect to BCS, BDDCS, and regulatory guidances has been published (7).

Both BCS and BDDCS use the same criteria for solubility. Therefore, there is no difference in the basis between the two systems with respect to this parameter. As noted above, BDDCS predictions and classification are based on the intestinal permeability rate, not the extent of permeability. There is some ambiguity with respect to the basis for BCS, as reviewed by Benet and Larregieu (6). The initial permeability studies of Amidon, Lennernäs, and colleagues (5,8), as summarized by Takagi *et al.* (3), show a good correlation between human intestinal permeability rate and the extent of absorption, as detailed earlier in the first paragraph of this paper. However, the criterion listed in the FDA BCS Guidance (4) is "…a drug substance is considered to be *highly permeable* when the extent of absorption in humans is determined to be 90% or more of an administered dose based on a mass balance determination or in comparison to an intravenous reference dose" [emphasis added by the FDA]. Although permeability rate methods are listed in the FDA BCS Guidance (4), we are unaware of any drug that has been certified by the FDA as class 1 eligible for *in vivo* biowaiver where there is no confirmatory ≥90% absorption data. This ambiguity does not exist in the Guideline on the Investigation of Bioequivalence issued in 2010 by the European Medicines Agency (EMA), which only allows *in vivo* biowaivers based on the extent of absorption (9). This difference in the permeability basis between BCS and BDDCS is brought home in a recent publication by FDA scientists (10). Chen and Yu (10) note that the FDA has classified as "highly permeable" a number of drugs where absorption is ≥90% in humans, but the measured permeability rates of these compounds are less than that for metoprolol (cefadroxil, cephradine, levofloxacin, loracarbef, ofloxacin, and sotalol), and in one case (pregabalin), the measured permeability rate is less than that for mannitol. As previously recognized (3), BCS is influenced by transporter effects. For example, large amino acid transporter-1 (LAT-1) is expressed in Caco-2 cells (11), and pregabalin is a LAT-1 substrate as noted in the package insert (12), which may explain this discrepancy. Since pregabalin is a zwitterion, its high oral bioavailability (≥90%) may be attributed to LAT-1 transport, an effect that is not taken into account by BCS. Thus, although in general drugs exhibiting high intestinal permeability rates show a high extent of absorption and a high extent of metabolism in both BCS and BDDCS, there are a number of drugs that could be classified as highly permeable in the BCS system based on absorption ≥90% but would be predicted to be poorly metabolized based on the low intestinal permeability rate, the basis for BDDCS classification. By evaluating metabolism, not permeability, BDDCS is not subject to variability due to transporter effects.

In general, classification of drugs between BCS and BDDCS only differ about 5–10%. However, for class 1 drugs where FDA has granted biowaivers, we estimate that the difference between BCS and BDDCS occurs for about 40% of drugs. We cannot make a more accurate estimate since the listing of all drugs granted biowaivers by the FDA is confidential. The percentage difference is high due to the ease in determining whether a drug is >90% absorbed (class 1 in BCS) when a drug is almost completely eliminated unchanged in the urine (class 3 in BDDCS).

BDDCS AND ITS USE

In 1995, Wu and Benet (1) reviewed 131 drugs that had been classified into the four BCS categories in the literature through the end of 1994. Ten of these drugs had been listed in different classes by different authors. Wu and Benet (1) recognized that the major route of elimination in humans for the great majority of high-permeability class 1 and class 2 drugs was metabolism, while the major route of elimination for the poorly permeable class 3 and class 4 drugs in humans was renal and biliary excretion of unchanged drug. They also noted that the major route of elimination via cytochrome P450 3A4 (CYP3A4) was only observed for the class 1 and class 2 drugs and that for the class 3 and class 4 drugs CYP3A4 was not a major contributor to elimination for any. Since the extent of metabolism is better characterized than the extent of absorption, for marketed drugs, Wu and Benet proposed that in BDDCS, drugs be categorized in terms of the extent of metabolism and solubility *versus* permeability rate and solubility (1). This immediately eliminated the situation where drugs were classified in more than one class because of the uncertainty of permeability measures from study to study. The implication from the BDDCS for an NME is that if a surrogate measure of intestinal absorption rate is available, such as permeability rate through a Caco-2 cellular system, it would be possible to predict the major route of elimination for this new molecular entity in humans prior to its *in vivo* dosing to either animals or humans. Work is ongoing in our laboratory to determine the degree of accuracy in predicting BDDCS class for an NME based only on *in vitro* permeability measures prior to studies determining the extent of metabolism. Thus, Benet and Wu (1) proposed the BDDCS as shown in Fig. 1 with ≥70% metabolism being the cutoff for extensive metabolism. They also noted that there were relatively few drugs where the extent of metabolism was between 30% and 70% and that most drugs are either very highly metabolized or very poorly metabolized.

Figure 2 summarizes the predictions from BDDCS related to the effects of enzymes and transporters in the gut and liver following oral dosing of drugs (1,13). For class 1, highly soluble—high permeability rate—extensively metabolized drugs, transporter effects in the intestine and the liver have no clinical impact. Even compounds like verapamil,

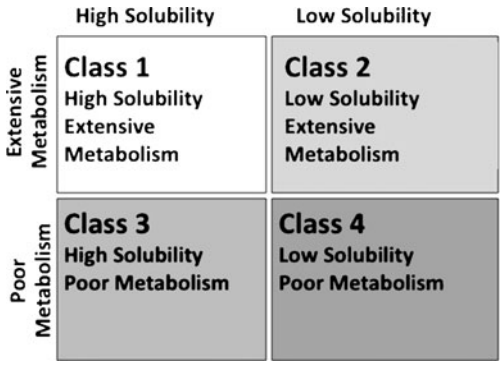

Fig. 1. The Biopharmaceutics Drug Disposition Classification System (BDDCS) as proposed by Wu and Benet (1)

which can be shown in certain cellular systems (*e.g.*, MDR1-MDCK) to be a substrate for P-glycoprotein (P-gp), exhibit no clinically significant P-gp substrate effects in the gut and the liver. Thus, a major proposition of BDDCS is that although class 1 drugs may be shown in cellular systems to be substrates for transporters found in the intestine and the liver, this has no clinical relevance. However, a caution is in order here. At this time, BDDCS predictions only apply to the intestine and the liver since class 1 drugs could be substrates for transporters at the blood–brain barrier and in the kidney.

From Fig. 2, it can be seen that for class 2 drugs, efflux transporter effects will predominate in the intestines. Thus, transporter–enzyme interplay will be primarily important for class 2 compounds that are substrates for CYP3A and phase II gut enzymes (*e.g.*, glucuronosyltransferases, sulfotransferases), where efflux transporter effects can control the access of the drug to the gut enzymes. BDDCS predicts that both uptake and efflux transporters can affect class 2 drug disposition in the liver. Thus, inhibition or induction of uptake hepatic transporters such as the SLCOs (OATPs) and the SLC22As (OATs and OCTs) as well as the drug efflux hepatic transporters ABCB1 (P-gp), ABCG2 (BCRP), and ABCCs (MRPs) can lead to changes in hepatic metabolism even when hepatic enzymes are unaffected.

BDDCS predicts that for class 3, highly soluble—poor permeability rate—poorly metabolized drugs, uptake transporters will be important for intestinal absorption and liver entry for these poorly permeable compounds (Fig. 2). However, once these drugs get into the enterocyte or the hepatocyte, efflux transporter effects can also occur. Similarly, uptake and efflux transporter effects would be expected for the poorly soluble class 4 compounds. Because they are numerically underrepresented, one might expect that class 4 drugs are more difficult to manage therapeutically, *i.e.*, there are transporter effects just as in class 2, except these drugs are not significantly metabolized. As will be shown subsequently, plotting the maximum recommended therapeutic daily dose (14) *versus* BDDCS and looking at the "actives" (low dose) *versus* "inactives" (high dose, safer) revealed no such relationship. It is more likely that fewer drugs are represented in class 4 because of the combined negative characteristics of high dose and (comparatively) low solubility, which leads to high variability. Since the FDA criteria for solubility is measured in water, we suspect that the approved class 4 drugs have adequate solubility in the natural surfactant containing intestinal fluids.

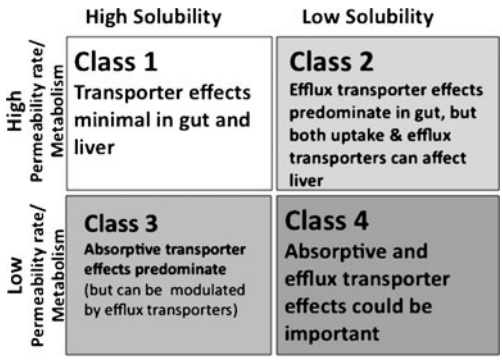

Fig. 2. Transporter effects predicted by BDDCS following oral dosing

Details and explications for the predictions in Fig. 2 have been presented in recent reviews from the Benet lab (13,15,16). However, in large part, the predictions in Fig. 2 were based on clinical and experimental observations. That is, we are unaware of any clinically significant effects of the uptake and efflux transporters in the gut and liver on class 1 drugs, even when such drugs have been shown in cellular systems or other organs besides the gut and the liver to be substrates of the uptake and efflux transporters. These effects, however, might become relevant in overdosage situations, *e.g.*, when combined with strong inhibitors of their respective metabolizing enzyme, when liver failure is manifest, or when accidentally overdosed. Similarly, we are unaware of the clinically significant effects of the uptake transporters in the gut for class 2 drugs even when these drugs are shown to be substrates of uptake transporters in the liver.

BDDCS also allows potential drug–drug interactions to be predicted (16,17). For class 1 drugs, only metabolic interactions need to be considered in the intestine and the liver. For class 2 drugs, metabolic, efflux transporter, and efflux transporter–enzyme interplay in the intestine must be taken into consideration, while in the liver, metabolic, uptake transporter, efflux transporter, and transporter–enzyme interplay (both uptake and efflux) can occur. For class 3 and class 4 drugs, uptake transporter, efflux transporter, and uptake–efflux transporter interplay will be of major importance.

BDDCS classification may also be useful in predicting the effect of high-fat meals on the extent of bioavailability (F) for an NME. In general, F for class 1 drugs is unaffected by high-fat meals; F is generally increased for class 2 drugs and generally decreased for class 3 drugs (18). Custodio *et al.* (19) have observed that these findings would be the outcomes expected if a component of high-fat meals inhibited both the uptake and efflux transporters. However, even if this were true, high-fat meals would be expected to have many other effects than inhibiting transporters. We estimate that the predicted effect of high-fat meals on F is only correct about 70% of the time.

CAUTION

It is surprising that such a simple four-category process as indicated in Fig. 2 works so well in predicting drug disposition, transporter–enzyme effects, and drug interac-

tions. It is obvious, however, that this simple four-category system will not predict every interaction. BDDCS does not propose that every drug in the class will be substrates or not substrates for the uptake and efflux transporters. Rather, BDDCS helps prioritize what interactions should and should not be investigated. For example, the class 2 drug felodipine has been shown not to be affected by the intestinal or hepatic efflux transporters (20). Recently, our laboratory has shown the importance in humans of hepatic uptake transporters for the drugs atorvastatin and glyburide (21,22). These interactions were predicted based on cellular, isolated organ, and animal studies (22–24). Even when such preliminary studies confirm BDDCS predictions, this may not always be the case. Warfarin is a class 2 drug and, thus according to BDDCS, may be a substrate for a hepatic uptake transporter. *In vitro* studies in human and rat hepatocytes showed that rifampin would decrease warfarin metabolism by 30% (25), a similar extent to that found for our *in vitro* results with glyburide (22). However, our recently published study examining the effects of a single dose of rifampin on the pharmacokinetics of warfarin in healthy volunteers showed that OATP uptake *in vivo* in humans was not clinically significant for warfarin (25). Similarly, although warfarin appears to be both a substrate and inhibitor of liver-bound P-gp (26), this has not been regarded as clinically significant; one P-gp haplotype, however, is clearly associated with low-dose warfarin in a 201 patient sample (27). This emphasizes again the caution that BDDCS only predicts with respect to transporters what might occur, but not that the effect will always occur. Furthermore, our example above (25) reinforces the well-recognized concept that observations in cellular systems and animal models must be tested *in vivo* in humans before the significance of the effect is assumed.

WHY DID WE PREPARE THIS PAPER?

Wu and Benet (1) recognized that the FDA's BCS approach (4) held the potential for predicting the drug disposition characteristics and drug interactions for NMEs as well as for drugs on the market. The use of BDDCS in the area of systems chemical biology (28) has been previously outlined (29), and computational models to assign BDDCS class from molecular structure have been proposed (30). However, to test the usefulness of BDDCS, to examine patterns within the BDDCS classes and among them, and to gain further perspectives, it is necessary to compile a large database, at least with respect to drugs that have reached the market. Since BDDCS makes predictions related to hepatic elimination in addition to intestinal absorption, such a database should include as many drugs as possible where systemic concentrations are relevant. Thus, approximately one quarter of the drugs categorized here are administered exclusively by non-oral routes. We also felt strongly that the information provided in the database should be based, where available, not only on the *in silico* predictions of those parameters but also on experimental values. We noted that many of the solubility values used in BCS analyses are frequently *in silico* predictions of solubility. For example, in the often quoted paper of Willmann *et al*. (31) describing a physiological model for the estimation of the fraction dose absorbed in humans, the measured solubility values were only included for only 22 of the 126 drugs evaluated. The solubility for the great majority of the drugs utilized in the Willmann *et al*. (31) analysis came from the compilation of Zhao *et al*. (32). These latter workers evaluated human intestinal absorption data for 241 drugs (32). Of the 241 drugs, Zhao *et al*. compared the experimental results for 26 of the compounds with the predicted solubility utilizing the method of Meylen *et al*. (33) based on octanol water partition coefficients. For these 26 drugs, the measured *versus* calculated solubility differs by a factor of 5.7±6.0-fold, the greatest difference being 23-fold. Thus, at present, *in silico* methodologies for aqueous solubility prediction are not sufficiently accurate for the BDDCS analysis not only due to the inherent limitations of such methods but also to its definition, *i.e.*, BDDCS solubility categorization depends on the maximum strength dose and the effect of pH. Experimental solubility values were included in this compilation wherever they could be found in the literature (577 drugs). Qualitative evaluations such as "practically insoluble in water," which relate to upper limits, and "highly soluble in water" were used in the absence of published solubility values from a reliable source and were the basis of the BDDCS assignment when no measured value is listed in the table.

Frequently, large compilations such as the ones presented here are carried out with the assistance of graduate students, postdoctoral fellows, and auxiliary personnel. In our experience, this can lead to unevenness in the quality of the data presented in the table. For each of the drugs listed here, decisions concerning the experimental values to be listed and classification assigned were made during the multiple joint meetings of Drs. Benet and Oprea between February 2007 and February 2011. Then, Dr. Broccatelli captured potential errors by cross-checking many references. Therefore, if there are errors in the parameters or in the assignments, this can only be attributable to the authors.

MEASURED PARAMETERS (IN ORDER OF DIFFICULTY)

Solubility

There are a number of issues concerning the choice of the high *versus* low solubility criteria and which representative experimental values should be listed. The high solubility criterion that the highest dose strength on the market is soluble in 250 mL or less of water over the pH range 1–7.5 at 37°C was an arbitrary decision made by Amidon *et al*. (5) and incorporated into the regulatory Guidances (4,9). Wu and Benet (1) found that this cutoff criterion in BCS appeared to work well for BDDCS, and thus, we have continued to use this arbitrary, discriminatory criterion. The FDA criteria (4) require the solubility measurements to be made in water, not simulated intestinal fluid containing a surfactant, and the solubility values listed in the table are values in water. Furthermore, the FDA criteria evaluate the cutoff between high and low solubility using the value for the lowest solubility over the pH range 1–7.5 (realistically measured at pH 1.2, 4.5, and 6.8 as indicated in the FDA Guidance). Furthermore, the solubility is to be measured at 37°C. The values in Tables I, II, III, IV, and V are the authors' best recommendation based on experimental literature data for

Table I. Measured and *In Silico* Data for 351 BDDCS Class 1 Drugs

Generic name	Maximum strength dose value	Maximum strength dose unit	Formulation	Route	Measured solubility (mg/mL)	Dose number	% Excreted unchanged in urine	MW drug	Measured Log*S* molar	Measured Log*P*	Measured LogD_{74}	minVSLgS 3–7.5	CLog*P*	HBA	HBD	PSA
Abacavir sulfate	300	mg	Tablets	Oral	77	0.02	1.2	286.34	−0.57	1.20	1.20	−3.07	0.81	6	3	95.80
Acarbose	100	mg	Tablets	Oral			1	645.62		−8.83		3.30	−6.66	19	14	351.80
Acebutolol hydrochloride	400	mg	Capsules	Oral			10	336.43		1.71	0.19	−1.46	1.71	5	3	97.05
Acetaminophen; paracetamol	1000	mg	Tablets	Oral	23.7	0.2	3	151.17	−0.80	0.20	0.40	−1.66	0.49	2	2	55.41
Acetohexamide	500	mg	Tablets	Oral	3.43	0.6		324.40	−1.98	2.44	−0.36	−3.13	2.25	4	2	103.22
Acetylsalicylic acid; aspirin	500	mg	Tablets	Oral	10	0.2	1.4	180.16	−1.26	1.19	−2.57	−0.94	1.02	3	1	68.21
Adenosine	3	mg/mL	Solution	Injection (i.v.)	5		0	267.25	−1.73	−0.98	−1.10	−1.37	−2.16	8	4	135.44
Alfacalcidol	1	μg	Capsules	Oral			8	400.65				−5.86	8.24	2	2	45.12
Alfentanil	0.5	mg/mL	Solution	Injection (i.v.)			0.5	416.53		2.16	2.10	−4.12	2.13	6	0	77.73
Alfuzosin	10	mg	Tablets	Oral			11	389.46			−1.18	−3.80	2.55	8	2	108.88
Aliskiren	300	mg	Tablets	Oral	350	0.003	25	551.77	−0.20		2.45	−3.09	3.51	7	4	156.62
Alosetron	1	mg	Tablets	Oral	61	0.00007	6	294.36	−0.68			−3.26	1.74	2	1	44.23
Alprazolam	2	mg	Tablets	Oral	0.073	0.1	20	308.77	−3.63	2.12	1.26	−3.68	2.56	3	0	33.27
Alprenolol	200	mg	Tablets	Oral	50	0.02	0.5	249.36	−0.70	3.10	1.34	−0.86	2.65	3	2	46.24
Ambrisentan	10	mg	Tablets	Oral	0.06	0.7	5	376.46	−3.80			−3.35	3.33	5	1	70.11
Ambroxol	30	mg	Tablets	Oral	10.9	0.01	8	364.08	−1.52			−2.44	2.66	3	3	64.50
Amifostine	5	mg/mL	Solution	Injection (i.v.)			0.69	214.22		−1.04		3.12	−1.85	5	4	106.66
Aminophenazone; aminopyrine	300	mg	Tablets	Oral	55.55	0.02		231.30	−0.62		1.00	−2.23	1.04	3	0	26.79
Amitriptyline hydrochloride	150	mg	Tablets	Oral	1000	0.0006	1	277.41	0.50	4.92	2.95	−2.29	4.85	1	0	1.18
Amlodipine	10	mg	Tablets	Oral			10	408.89		3.00	1.68	−1.79	3.43	5	2	105.47
Amoxapine	150	mg	Tablets	Oral				313.79				−2.43	3.41	3	1	34.47
Amsacrine	33.33	mg/mL	Solution	Injection (i.v.)			10	393.47				−1.37	4.69	5	2	85.11
Anastrozole	1	mg	Tablets	Oral	0.5	0.008	10	293.37	−2.77			−3.60	1.29	4	0	61.36
Anhydrovinblastine; anhydrovincaleukoblastine	1	mg/mL	Solution	Injection (i.v.)	10	0.0004	0.5	792.98	−1.90	3.70	3.69	−7.12	6.11	8	2	130.05
Antipyrine; phenazone	500	mg	Tablets	Oral	1700	0.001	0.5	188.23	0.96		0.28	−1.79	0.20	2	0	22.02
Apomorphine	2.56	mg	Tablets	Injection (s.c.)	20	0.0005	0.3	267.33	−1.13	2.30		−2.73	2.49	3	2	46.92
Asenapine	10	mg	Tablets	Oral			1	285.78				−2.41	4.58	1	0	10.59
Atomoxetine	60	mg	Capsules	Oral	27.8	0.009	1.5	255.36	−0.96			−1.14	3.94	2	1	23.68
Azathioprine	100	mg	Tablets	Oral	10	0.04	1	277.27	−1.44	0.10	0.02	−2.72	0.51	6	1	99.66
Bambuterol	20	mg	Tablets	Oral	33	0.002	0	367.45	−1.05	1.50	−2.58	−1.56	0.56	4	2	94.24
Benazepril	40	mg	Tablets	Oral	78	0.002	0.5	424.50	−0.74		1.10	−1.84	1.82	5	2	101.61
Bendamustine	5	mg/mL	Solution	Injection (i.v.)			1	358.27				−0.83	2.76	4	1	69.78
Benidipine	8	mg	Tablets	Oral	1.9	0.02	1	535.65	−2.45			−5.69	7.41	0	0	112.85
Benserazide	50	mg	Tablets	Oral			1	257.25				2.13	−2.90	7	7	169.84
Benznidazole	100	mg	Tablets	Oral	0.4	1.0		260.25	−2.81			−2.65	0.90	4	1	87.81
Bepridil	400	mg	Tablets	Oral	5	0.3	0.5	366.55	−1.87		2.00	−4.29	6.20	3	0	10.84
Beraprost	0.04	mg	Tablets	Oral	19	0.000008		398.50	−1.32			−4.64	2.04	5	3	95.05
Betamethasone	5	mg	Tablets	Oral	0.066	0.3	4.8	392.47	−3.77	1.94	1.94	−3.61	1.79	5	3	104.22
Betaxolol	20	mg	Tablets	Oral	0.451	0.2	15	307.44	−2.83	2.81	0.55	−1.66	2.32	4	2	55.03
Bimatoprost	0.30	mg/mL	Solution	Ophthalmic	0.8			415.58	−2.72			−5.44	1.75	4	4	100.52
Biperiden	2	mg	Tablets	Oral	1	0.008		311.47	−2.49	4.25		−1.93	4.94	2	1	23.73
Bopindolol	2	mg	Tablets	Oral	3.3	0.002	0	380.49	−2.06		4.22	−3.92	4.98	3	2	64.71
Bortezomib	1	mg/mL	Solution	Injection (i.v.)	3.3			384.25	−2.07			−4.09	0.78	6	4	151.53
Brimonidine	2	mg/mL	Solution	Ophthalmic	1.5		10	292.14	−2.29	0.78		−2.00	1.49	5	2	58.94
Bromazepam	6	mg	Tablets	Oral	0.17	0.1		316.16	−3.27	2.05	1.54	−3.47	1.70	3	1	52.40
Bromocriptine	5	mg	Capsules	Oral	0.8	0.03	2	654.61	−2.91		4.59	−6.80	6.58	6	3	118.24
Bromperidol	10	mg	Tablets	Oral	0.09	0.4	0.5	420.33	−3.67	2.74	3.34	−3.84	4.00	3	1	42.01
Budesonide	3	mg	Capsules	Oral	0.02	0.6	0	430.55	−4.33	3.20	2.70	−4.71	2.91	6	2	99.25
Buflomedil hydrochloride	300	mg	Tablets	Oral			23.6	307.39			−0.75	−1.23	2.93	5	0	46.76
Bupivacaine	5	mg/mL	Solution	Injection (epidural)	0.17		2	288.44	−3.23	3.41		−3.53	3.69	2	1	33.72
Buprenorphine hydrochloride	8	mg	Tablets	Oral	17	0.002	1	467.65	−1.47	4.98		−3.58	3.99	5	2	64.50
Bupropion	100	mg	Tablets	Oral	312	0.001	0.5	239.75	0.11		3.27	−1.99	3.21	2	1	32.84
Busulfan (busulphan)	2	mg	Tablets	Oral	0.1	0.08	1	246.30	−3.39	−0.52	−0.52	−1.20	−0.59	4	0	92.04

Table I. (Continued)

Generic name	Maximum strength dose value	Maximum strength dose unit	Formulation	Route	Measured solubility (mg/mL)	Dose number	% Excreted unchanged in urine	MW drug	Measured LogS molar	Measured Log*P*	Measured LogD_{74}	minVSLgS 3–7.5	CLog*P*	HBA	HBD	PSA
Butabarbital	100	mg	Tablets	Oral			1	212.25		1.65	1.45	−2.42	1.58	3	2	83.96
Butalbital	50	mg	Tablets	Oral			3.6	224.26				−2.74	1.63	3	2	83.96
Butorphanol	5	mg	Tablets	Oral	2	0.01	2	327.47	−2.21	2.26		−2.40	3.73	3	2	46.61
Caffeine	65	mg	Caplets	Oral	21.5	0.01	1	194.19	−0.96	−0.07	−0.07	−1.95	−0.04	3	0	48.50
Capecitabine	500	mg	Tablets	Oral	26	0.08	3	359.36	−1.14			−3.45	0.84	6	3	124.33
Caprylidene	20000	mg	Powder	Oral			0	470.70				−7.69	9.97	3	0	81.19
Carbidopa	25	mg	Tablets	Oral	2.5	0.04	5.3	226.23	−1.96			1.33	−0.45	6	5	132.39
Carmustine	7.70	mg	Implant	Topical (skin, membranes)	3.8	0.008	0.5	214.05	−1.75	1.53	1.53	−2.50	1.32	2	1	69.78
Caspofungin acetate	6.48	mg/mL	Solution	Injection (i.v.)			1.4	1093.34				−3.18	−2.95	18	16	454.42
Cefoperazone	2000	mg	Powder	Injection (i.v.)			29	645.68		−0.74	−2.12	−3.47	−0.22	11	4	227.75
Cerivastatin	0.8	mg	Tablets	Oral	195	0.00002	24	459.56	−0.37			−2.00	3.56	6	3	104.98
Cetrorelix	3	mg/mL	Solution	Injection (s.c.)	8		3	1431.07	−2.25			−7.00	−0.40	18	17	543.33
Cevimeline	30	mg	Capsules	Oral			13.5	199.32				−1.32	1.14	2	0	9.97
Chloral hydrate	500	mg	Capsules	Oral	8300	0.0002		165.40	1.70	0.99	1.61	−0.77	0.72	2	2	45.12
Chlorambucil	2	mg	Tablets	Oral	12	0.0007	0.5	304.22	−1.40	3.25	1.59	−0.27	3.63	3	1	41.70
Chloramphenicol	250	mg	Capsules	Oral	2.5	0.4	5	323.13	−2.11	1.14	1.00	−2.79	1.28	5	3	122.11
Chlordiazepoxide	25	mg	Capsules	Oral	2	0.05	0.5	299.76	−2.18	2.44	2.19	−2.65	3.79	3	1	45.94
Chlormethiazole; clomethiazole	192	mg	Capsules	Oral	10	0.08	0.05	161.65	−1.21	2.12	2.12	−1.80	1.68	1	0	10.24
Chlorpheniramine	4	mg	Tablets	Oral			10	274.80		3.38	1.38	−1.57	3.15	2	0	11.42
Chlorpromazine	200	mg	Tablets	Oral	400	0.002	0.5	318.87	0.10	5.41	2.82	−2.69	5.30	2	0	1.75
Cilazapril	5	mg	Tablets	Oral	1	0.02	0	417.51	−2.62		−2.25	−0.78	1.47	6	2	106.36
Cisplatin	1	mg/mL	Solution	Injection (i.v.)	2.53		2.3	300.06	−2.07	−2.53			−1.68	0	2	75.29
Clemastine	2	mg	Tablets	Oral	2.3	0.003	5	343.90	−2.17	5.49	3.04	−2.56	5.45	2	0	9.97
Clindamycin hydrochloride hydrate	300	mg	Capsules	Oral	40	0.03	13	424.99	−1.08	2.16		−2.99	2.57	6	4	110.49
Clobazam	10	mg	Tablets	Oral	0.188	0.2		300.75	−3.20	2.12	1.90	−3.63	2.44	2	0	37.99
Clofibric acid		Active metabolite			45		5.7	214.65	−0.68	2.57	−1.13	−1.63	2.82	3	1	49.94
Clomiphene citrate	50	mg	Tablets	Oral	1.11	0.2	8	405.97	−2.73	6.70		−4.24	7.15	2	0	10.28
Clomipramine	75	mg	Tablets	Oral				314.86		5.19	2.76	−2.56	5.92	2	0	1.75
Clonazepam	2	mg	Tablets	Oral	0.1	0.08	0.5	315.72	−3.50	2.41	2.41	−3.96	2.38	4	1	86.30
Clorazepate	15	mg	Tablets	Oral			0.5	314.73			−1.13	−2.36	2.51	4	2	82.98
Cocaine	0.1	mg/mL	Solution	Topical (nasal)	1.6		1	303.36	−2.28	2.30	2.30	−2.85	2.57	3	0	55.30
Codeine monohydrate	60	mg	Tablets	Oral	435	0.0006	0.1	299.37	0.14	1.19	0.21	−1.40	0.98	4	1	41.94
Colchicine	0.6	mg	Tablets	Oral	45	0.00005		399.45	−0.95	1.30	1.03	−3.90	1.20	6	1	87.54
Cortisone	25	mg	Tablets	Oral	0.28	0.4		360.45	−3.11	1.47	1.47	−3.52	1.30	5	2	99.93
Cyanocobalamin (vitamin B12)	5	mg	Tablets	Oral	12.5	0.002	0.5	1355.40	−2.04			0.05	−1.36	17	9	492.69
Cyclizine	50	mg	Tablets	Oral	8.7	0.02	0.5	266.39	−1.49			−2.97	3.80	2	0	2.35
Cyclobenzaprine	10	mg	Tablets	Oral	200	0.0002	0.5	275.40	−0.14			−2.58	5.10	1	0	1.18
Cyclophosphamide	50	mg	Tablets	Oral	40	0.005	6.5	261.09	−0.81	0.63	0.63	−1.92	0.80	2	1	44.31
Cyproheptadine	4	mg	Tablets	Oral	3.636	0.004	0.5	287.41	−1.90	4.69		−3.19	5.30	1	0	1.18
Cytarabine	20	mg/mL	Solution	Injection (i.v.)			11	243.22		−2.51	−2.24	−0.60	−2.20	7	4	133.23
Dabigatran etexilate	110	mg	Capsules	Oral	1.8	0.2	0	627.75	−2.54	3.80		−7.74	4.13	8	2	146.19
Dantrolene	100	mg	Capsules	Oral	2	0.2	5	314.26	−2.20	1.70	0.77	−3.44	1.63	5	1	118.74
Darifenacin	15	mg	Tablets	Oral			12.5	426.56				−3.74	3.62	3	1	56.52
Debrisoquine	20	mg	Tablets	Oral	29	0.003	12	175.24	−0.78	0.75	−2.96	2.59	0.90	3	2	52.16
Desalkylflurazepam		Active metabolite					0.5	288.71		2.70	2.78	−3.78	2.81	2	1	42.15
Desipramine	200	mg	Tablets	Oral			2	266.39		4.90	1.40	−0.80	4.47	2	1	15.14
Desmethyldiazepam (nordazepam)	10	mg	Tablets	Oral	0.057	0.7	0.5	270.72	−3.68	2.93	2.93	−3.69	3.02	2	1	42.15
Desogestrel	1.5	mg	Tablets	Oral	0.32	0.02	0	310.48	−2.99			−4.86	5.68	1	1	22.56
Dexamethasone	0.75	mg	Tablets	Oral	0.092	0.03	2.6	392.47	−3.63	1.94	1.83	−3.65	1.79	5	3	104.22
Dexmethylphenidate	10	mg	Tablets	Oral			0.5	233.31		1.80	−0.28	−1.61	2.56	2	1	41.64

Dextromethorphan hydrobromide	60	mg	Tablets	Oral	15	0.02	0.19	271.41	−1.26			−1.35	3.95	2	0	10.28
Dezocine	15	mg/mL	Solution	Injection (i.v.)	20		1	245.37	−1.09		1.12	−0.65	3.72	2	2	50.84
Diazepam	10	mg	Tablets	Oral	0.057	0.7	0.5	284.75	−3.70	2.82	2.99	−3.75	2.96	2	0	28.76
Diclofenac	50	mg	Tablets	Oral	9	0.02	0.5	296.16	−1.52	4.51	1.13	−3.43	4.73	3	2	54.80
Dihydroquinidine; hydroquinidine	300	mg	Tablets	Oral	11.1	0.1	18	326.44	−1.51	3.44	1.82	−2.61	3.27	6	3	43.08
Dilevalol	50	mg	Tablets	Oral	16		2.5	328.41	−1.31	3.09	1.07	−2.09	2.50	4	4	106.25
Diltiazem	120	mg	Capsules	Oral			2	414.53		2.70	2.22	−3.77	3.65	4	0	56.49
Diphenhydramine	50	mg	Capsules	Oral	1000	0.0002	2	255.36	0.59	3.27	1.61	−1.84	3.45	2	0	9.97
Dobutamine hydrochloride	12.5	mg/mL	Solution	Injection (i.v.)			0.1	301.39				−1.85	2.43	4	4	83.19
Dolasetron	100	mg	Tablets	Oral			0	324.38				−1.96	2.34	3	1	60.48
Dosulepin; dothiepin	75	mg	Tablets	Oral	500		5	295.45	0.23	4.49	2.76	−2.26	4.53	1	0	1.18
Doxazosin	8	mg	Tablets	Oral				451.49			0.60	−4.55	3.53	9	1	104.90
Doxepin	100	mg	Capsules	Oral			0	279.39		4.29	2.37	−2.30	4.09	2	0	10.28
Doxorubicin	2	mg/mL	Solution	Injection (i.v.)	10		3.5	543.53	−1.74	1.27	1.27	−3.74	0.32	12	6	222.89
Duloxetine hydrochloride	67.3	mg	Capsules	Oral			0	297.42				−2.22	4.26	2	1	23.68
Eletriptan hydrobromide	40	mg	Tablets	Oral	4	0.04	5	382.53	−1.98		1.10	−2.30	3.36	3	1	51.90
Enalapril	20	mg	Tablets	Oral	25	0.003	10	376.46	−1.18			−0.67	0.67	5	2	101.91
Enfuvirtide	90	mg/mL	Solution	Injection (i.m.)	1000		0	4491.98	−0.65					67	63	2095.89
Epirubicin	2	mg/mL	Solution	Injection (i.v.)			9.5	543.53		1.27	0.46	−3.77	0.32	12	6	222.89
Ergonovine; ergometrine	0.2	mg	Tablets	Oral	10	0.00008		325.41	−1.51			−3.07	1.23	3	3	70.55
Ergotamine tartrate	2	mg	Tablets	Oral	2	0.004		581.68	−2.82	3.69	2.85	−2.74	4.66	6	3	118.24
Escitalopram	20	mg	Tablets	Oral			8	324.40				−2.94	3.13	3	0	28.67
Esmolol	10	mg/mL	Solution	Injection (i.v.)	20		0.5	295.38	−1.17			−0.80	1.72	4	2	73.30
Esomeprazole magnesium	20	mg	Tablets	Oral	0.5	0.2	0.5	345.42	−2.84	2.23		−3.69	2.57	5	1	71.04
Estradiol	2	mg	Tablets	Oral	0.09	0.09	0.5	272.39	−3.48	4.01		−3.90	3.78	2	2	45.43
Eszopiclone	3	mg	Tablets	Oral			5	388.82				−2.82	1.25	6	0	79.29
Ethanol	62	mg/mL	Solution	Oral			2.5	46.07		−0.31	−0.31	1.06	−0.24	1	1	22.56
Ethinylestradiol	1	mg	Tablets	Oral			3	296.41		3.67	3.67	−4.16	3.86	2	2	45.43
Ethosuximide	250	mg	Capsules	Oral	39.2	0.03	25	141.17	−0.56	0.38	1.13	−1.24	0.40	2	1	51.12
Etonogestrel	157	μg	Tablets (and 68 mg implant s.c)	Topical (skin. membranes)	0.51	0.001	0.1	324.47	−2.80			−4.61	5.68	2	1	22.56
Everolimus	1	mg	Tablets	Oral	0.01	0.4	0	958.25	−4.98			−8.68	7.10	13	3	212.97
Exenatide	0.25	mg/mL	Solution	Injection (s.c.)	25			4186.66	−2.22				1.61	67	58	1923.78
Famciclovir	500	mg	Tablets	Oral	250	0.008	0	321.34	−0.11			−2.79	0.09	6	1	113.10
Fentanyl	1.6	mg	Lozenge	Oral	25	0.0003	8	336.48	−1.13	4.05	2.92	−3.65	3.62	2	0	20.32
Fesoterodine	8	mg	Tablets	Oral	256	0.0001	0	411.59	−0.21			−1.83	4.36	3	1	51.11
Finasteride	5	mg	Tablets	Oral	0.043	0.5	0.5	372.56	−3.94	3.03	3.03	−4.38	3.01	2	2	65.69
Fludarabine		Active metabolite					24	285.24		−0.80	−2.32	−1.68	−2.01	8	4	135.44
Fludarabine 5′-monophosphate	10	mg	Tablets	Oral	3.53	0.01		365.22	−2.01			0.64	−3.07	8	4	185.94
Fludrocortisone acetate	0.1	mg	Tablets	Oral	0.14	0.003	1	422.50	−3.48	1.67	1.67	−4.00	1.54	5	2	104.22
Flumazenil	0.1	mg/mL	Solution	Injection (i.v.)	0.128		0.5	303.30	−3.37	1.00	0.87	−3.34	1.29	3	0	57.02
Flunitrazepam	1	mg	Tablets	Oral	0.004	1.0	0.5	313.29	−4.89	2.06	2.06	−3.53	1.78	4	0	72.91
Fluorouracil	25	mg/mL	Solution	Injection (i.v.)	12.2		5	130.08	−1.03	−0.89	−0.89	−0.62	−0.58	2	2	64.48
Fluoxetine	20	mg	Capsules	Oral	15.2	0.005	1.25	309.33	−1.31	4.05	1.95	−1.19	4.57	2	1	23.68
Flurazepam	30	mg	Capsules	Oral	500	0.0002	0.1	387.89	0.11	3.94	2.35	−3.52	4.22	3	0	29.93
Fluvastatin sodium	40	mg	Capsules	Oral	50	0.003	1.5	411.48	−0.92	3.80		−4.00	4.05	4	3	86.52
Fluvoxamine	100	mg	Tablets	Oral	14.869	0.03	2	318.34	−1.33	1.12	1.21	−1.68	3.32	4	1	58.37
Formoterol fumarate	12	μg/inhalation	Powder	Topical (aerosol)	0.66	0.00007	8	344.41	−2.72			−2.00	1.26	5	4	101.65
Fosfluconazole	100	mg	Tablets	Oral				386.26			0.95	2.41	−0.78	7	2	120.98
Frovatriptan	2.5	mg	Tablets	Oral			6	243.31				0.42	0.72	2	3	74.79
Galantamine	12	mg	Tablets	Oral	10	0.005	20	287.36	−1.46			−1.09	1.03	4	1	41.94
Gemcitabine hydrochloride	40	mg/mL	Solution	Injection (i.v.)	15		8	263.20	−1.24			−0.97	−0.71	6	3	110.67
Glibornuride	25	mg	Tablets	Oral	0.2	0.5	0.5	366.48	−3.26	2.60	3.53	−3.75	3.70	4	3	107.50
Goserelin	10.8	mg	Implant	Injection (s.c.)			20	1269.44				−5.55	−2.86	18	18	537.10
Granisetron	1	mg	Tablets	Oral	100	0.00004	11	312.42	−0.49		−0.85	−1.16	1.72	3	1	47.74
Guanabenz	16	mg	Tablets	Oral	11	0.006		231.09	−1.32		0.12	−1.38	2.98	4	3	78.44
Heparin; enoxaparin	20	mg/mL	Solution (10,000 units/mL)	Injection (i.v.)	50		0.5	1134.94	−1.36			−3.81	−9.69	33	15	662.73

Table I. (Continued)

Generic name	Maximum strength dose value	Maximum strength dose unit	Formulation	Route	Measured solubility (mg/mL)	Dose number	% Excreted unchanged in urine	MW drug	Measured Log*S* molar	Measured Log*P*	Measured LogD_{74}	minVSLgS 3–7.5	CLog*P*	HBA	HBD	PSA
Hexobarbital	250	mg	Tablets	Oral	640	0.002	0.5	236.27	0.43	1.98	1.98	−2.81	1.63	3	1	70.56
Hydralazine hydrochloride	100	mg	Tablets	Oral	44.2	0.009	8	160.18	−0.65	1.00	0.56	−1.29	0.66	4	2	67.97
Hydrocodone	10	mg	Tablets	Oral	62.5	0.0006	10.2	299.37	−0.68	1.27	3.38	−1.25	1.13	4	0	37.66
Hydrocortisone; cortisol	20	mg	Tablets	Oral	0.42	0.2		362.47	−2.94	1.61	1.37	−3.48	1.70	5	3	104.22
Hydromorphone	8	mg	Tablets	Oral	10	0.003	6	285.35	−1.46			−1.06	0.72	4	1	51.42
Hydroxychloroquine sulfate	200	mg	Tablets	Oral	200	0.004	27	335.88	−0.23		1.72	−1.64	4.12	4	2	48.25
Hydroxyzine	100	mg	Tablets	Oral	700	0.0006	0.1	374.91	0.27	3.50	2.37	−3.76	4.00	4	1	33.70
Ibutilide	0.1	mg/mL	Solution	Injection (i.v.)	100		7	384.59	−0.58			−2.01	3.78	4	2	75.53
Idarubicin	1	mg/mL	Solution	Injection (i.v.)			3	497.51			1.63	−3.81	0.90	10	5	191.23
Ifosfamide	50	mg/mL	Solution	Injection (i.v.)	100		10	261.09	−0.42	0.86	0.86	−2.40	0.92	2	1	44.31
Iloprost	5	µg/inhalation	Solution	Topical (aerosol)	1	0.00002	0	360.50	−2.56	2.97	0.46	−4.40	2.71	4	3	85.95
Imidapril	10	mg	Tablets	Oral			5	405.45				−0.68	1.53	6	2	121.36
Imipramine	50	mg	Tablets	Oral			1.5	280.42		4.80	2.20	−2.04	5.04	2	0	1.75
Imiquimod	50	mg/g	Cream	Topical (skin. membranes)	0.6		1	240.31	−2.60			−2.71	3.24	3	1	48.73
Inamrinone; amrinone lactate	0.25	mg/mL	Solution	Injection (i.v.)	0.9		25	187.20	−2.49		−0.70	−1.89	−0.69	3	2	70.15
Indapamide	2.5	mg	Tablets	Oral	0.59	0.02	7	365.84	−2.79		2.09	−3.70	2.96	4	2	102.49
Irinotecan	20	mg/mL	Solution	Injection (i.v.)	10		16.7	586.69	−1.77			−3.79	2.73	6	1	108.44
Isoniazid	300	mg	Tablets	Oral	153	0.008	7	137.14	0.05	−0.70	−1.14	−0.67	−0.67	3	2	74.33
Isosorbide 2-mononitrate	10	mg	Tablets	Oral	1.1	0.04		191.14	−2.24	−0.40	−0.40	−0.83	−0.66	6	1	96.60
Isosorbide 5-mononitrate	20	mg	Tablets	Oral	1.1	0.07	2.5	191.14	−2.24	−0.40	−0.15	−0.88	−0.66	6	1	96.60
Isosorbide dinitrate	40	mg	Tablets	Oral	1.089	0.1		236.14	−2.34	1.31	1.31	−2.15	0.22	8	0	130.49
Ivabradine	7.5	mg	Tablets	Oral			4	468.60				−3.33	3.97	6	0	57.04
Ivermectin	3	mg	Tablets	Oral	4	0.003		875.12	−2.34		6.82	−8.48	5.39	13	3	173.88
Ketamine	100	mg/mL	Solution	Injection (i.v.)	200		4	237.73	−0.08	2.18	2.09	−1.35	2.93	2	1	32.84
Labetalol	300	mg	Tablets	Oral	16	0.08	2.5	328.41	−1.31	1.33	1.08	−2.14	2.50	4	4	106.25
Letrozole	2.5	mg	Tablets	Oral	0.041	0.2	3.9	285.31	−3.84			−4.71	1.24	4	0	61.36
Leuprolide	45	mg/mL	Solution	Injection (s.c.)	250		2	1209.43	−0.68			−5.36	−0.99	16	16	464.21
Levamisole	50	mg	Tablets	Oral				204.30		1.84	1.16	−1.62	1.84	2	0	10.79
Levobupivacaine	7.5	mg/mL	Solution	Injection (epidural)	0.17	0.2	0.5	288.44	−3.23	3.21	2.66	−3.53	3.69	2	1	33.72
Levodopa	250	mg	Tablets	Oral	1.65	0.6	0.5	197.19	−2.08	−2.74	−2.39	1.48	−2.82	5	4	114.54
Lidocaine	20	mg/mL	Solution	Injection (i.v.)	3.58		8	234.34	−1.82	2.44	1.88	−2.09	1.95	2	1	33.72
Linezolid	600	mg	Tablets	Oral	8	0.3	30	337.35	−1.62		1.80	−3.42	0.17	5	1	70.45
Liraglutide	6	mg/mL	Solution	Injection (s.c.)			6	3751.29						59	54	1675.18
Lorazepam	2	mg	Tablets	Oral	0.08	0.1	0.5	321.17	−3.60	2.39	2.39	−3.96	2.37	3	2	64.71
Lorcainide hydrochloride	100	mg	Tablets	Oral	2.4	0.2	1	370.93	−2.19	4.85	2.84	−2.88	4.48	2	0	20.32
Maprotiline	75	mg	Tablets	Oral	3.134	0.10	3	277.41	−1.95	4.85	1.43	−1.17	4.52	1	1	14.57
Maraviroc	300	mg	Tablets	Oral			8	513.68				−3.53	3.26	4	1	57.98
Melatonin	5	mg	Tablets	Oral	0.1	0.2		232.28	−3.37			−2.78	1.03	2	2	55.92
Melphalan	2	mg	Tablets	Oral	0.1	0.08	12	305.21	−3.48		−0.11	−0.39	−0.21	4	2	69.67
Meperidine; pethidine	100	mg	Tablets	Oral	3.22	0.1	13	247.34	−1.89	2.72	1.44	−1.65	2.23	2	0	28.24
Mepivacaine	20	mg/mL	Solution	Injection (epidural)	2.4		5	246.36	−2.01	1.95	1.75	−2.74	2.10	2	1	33.72
Meprobamate	400	mg	Tablets	Oral	3.4	0.5		218.25	−1.81	0.70	0.70	−1.53	0.92	2	2	110.07
Mesna	400	mg	Tablets	Oral				142.20				1.69	−1.55	3	2	59.79
Methadone	10	mg	Tablets	Oral	120	0.0003	24	309.46	−0.41	3.93	2.07	−2.46	4.17	2	0	19.45
Methohexital	10	mg/mL	Solution	Injection (i.v.)	100		0.5	262.31	−0.42		2.30	−3.13	1.81	3	1	70.56
Methylergonovine	0.2	mg	Tablets	Oral				339.44				−3.30	1.76	3	3	70.55
Methylphenidate	20	mg	Tablets	Oral				233.31		1.80	−0.28	−1.75	2.56	2	1	41.64
Methylprednisolone	32	mg	Tablets	Oral	0.3236	0.4	4.9	374.48	−3.06		2.18	−3.87	1.74	5	3	104.22
Metoprolol	100	mg	Tablets	Oral	1000	0.0004	10	267.37	0.57	1.88	0.16	−0.81	1.49	4	2	55.03
Metronidazole	500	mg	Tablets	Oral	10	0.2	10	171.16	−1.23	−0.02	0.14	−1.43	−0.46	4	1	77.52

Mexiletine	250	mg	Capsules	Oral			9.5	179.26		2.15	2.15	−0.12	2.57	2	1	37.08
Mianserin	60	mg	Tablets	Oral	3.4	0.07	5	264.37	−1.89	4.24	2.52	−2.73	3.76	2	0	2.05
Micafungin sodium	10	mg/mL	Solution	Injection (i.v.)			1	1270.30				−7.93	−2.59	22	16	554.51
Midazolam hydrochloride	2	mg/mL	Syrup	Oral	10.3		5.6	325.78	−1.55	3.27	1.53	−3.92	3.42	2	0	20.12
Minocycline hydrochloride	100	mg	Capsules	Oral	50	0.008	11	457.49	−0.96	0.05	0.04	2.53	0.19	9	5	175.38
Minoxidil	10	mg	Tablets	Oral	2.2	0.02	10	209.25	−1.98	1.24	1.38	−1.86	−0.72	5	2	89.15
Mirtazapine	45	mg	Tablets	Oral	0.5	0.4	2	265.36	−2.72			−2.31	2.81	3	0	12.29
Misoprostol	0.2	mg	Tablets	Oral			0.5	382.55			2.91	−5.01	3.07	4	2	90.45
Molindone	50	mg	Tablets	Oral			2	276.38				−1.77	2.57	3	1	42.21
Morphine hydrochloride	30	mg	Capsules	Oral	57.14	0.002	4	285.35	−0.75	0.89	1.03	−1.26	0.57	4	2	55.71
Nafarelin	0.2	mg/actuation	Solution	Topical (nasal)	1	0.0008	3	1322.50	−3.12			−5.45	−1.22	17	17	510.46
Nalbuphine hydrochloride	20	mg/mL	Solution	Injection (i.v.)	35.5		4	357.45	−1.00			−2.41	1.39	5	3	78.27
Nalmefene hydrochloride	1	mg/mL	Solution	Injection (i.v.)	124		9.6	339.44	−0.44		−1.13	−2.87	2.64	4	2	55.71
Naloxone	2	mg	Tablets	Oral			0	327.38		2.09	1.28	−2.14	0.16	5	2	73.98
Naltrexone	100	mg	Tablets	Oral	100	0.004	1	341.41	−0.53	1.92	0.90	−2.10	0.36	5	2	73.98
Nefopam	30	mg	Tablets	Oral	34	0.004	3	253.35	−0.87	3.00		−2.39	2.91	2	0	9.97
Niacin; nicotinic acid	1000	mg	Capsules	Oral	16.66	0.2		123.11	−0.87	0.36	−2.87	−0.05	0.80	3	1	51.07
Niacinamide; nicotinamide	750	mg	Tablets	Oral	1000	0.003		122.13	0.91			−1.01	0.80	2	1	56.49
Nicardipine	30	mg	Capsules	Oral	7.9	0.02	0	479.54	−1.78	3.82		−4.96	5.23	6	1	114.03
Nicorandil	20	mg	Tablets	Oral	4.2	0.02	0.5	211.18	−1.70		0.72	−1.98	0.75	5	1	99.54
Nicotine	4	mg	Tablets (as chewing gum)	Oral			16.7	162.24		1.17	0.43	−0.25	0.88	2	0	11.42
Nitroglycerin	0.4	mg	Tablets	Sublingual	0.8	0.002	0.5	227.09	−2.45	1.62	1.62	−2.68	1.76	9	0	169.35
Norethindrone	0.35	mg	Tablets	Oral	0.01	0.1	2	298.43	−4.47	2.97	2.97	−3.97	2.78	2	1	40.83
Norgestimate	0.25	mg	Tablets	Oral	0.02	0.05	0	369.51	−4.27		3.60	−5.17	5.06	3	1	62.44
Norgestrel	0.5	mg	Tablets	Oral	0.002	1.0	0	312.46	−5.19		3.60	−4.38	3.31	2	1	40.83
Nortilidine		Active metabolite					3	259.35				−2.48	3.16	2	1	41.64
Nortriptyline	75	mg	Capsules	Oral			2	263.39		4.04	1.69	−1.22	4.32	1	1	14.57
Octreotide acetate	1	mg/mL	Solution	Injection (i.v.)			32	1019.26				−4.53	2.51	12	13	367.50
Olmesartan medoxomil	40	mg	Tablets	Oral	2	0.08	0	558.60	−2.45			−3.53	2.91	8	2	150.96
Omeprazole	40	mg	Tablets	Oral	0.5	0.3	0	345.42	−2.84	2.23	2.23	−3.69	2.57	5	1	71.04
Ondansetron	8	mg	Tablets	Oral	5.7	0.006	5	293.37	−1.71		2.12	−3.18	2.72	2	0	29.66
Orphenadrine	100	mg	Tablets	Oral	10	0.04	8	269.39	−1.43	3.77	2.78	−2.18	3.90	2	0	9.97
Oseltamivir phosphate	75	mg	Capsules	Oral			2	312.41				−2.36	2.13	4	2	96.67
Oxaliplatin	5	mg/mL	Solution	Injection (i.v.)	6			395.29	−1.82			3.13	0.78	2	2	48.49
Oxprenolol	80	mg	Tablets	Oral	30.86	0.01	3	265.36	−0.93	2.10	0.18	−0.80	2.09	4	2	55.34
Oxybutynin hydrochloride	15	mg	Tablets	Oral	0.8	0.08	0.5	357.50	−2.69			−4.23	4.87	3	1	50.80
Oxycodone	80	mg	Tablets	Oral	100	0.003	19	315.37	−0.50	0.21	1.65	−1.64	−0.04	5	1	60.22
Oxymorphone	40	mg	Tablets	Oral	24	0.007	1.9	301.35	−1.10	0.90	0.98	−1.39	−0.48	5	2	73.98
p-Aminosalicylic acid (PAS)	1200	mg	Tablets	Oral	142.85	0.03	2	153.14	−0.03	0.89		−0.32	1.06	4	3	91.37
Pantoprazole sodium	40	mg	Tablets	Oral			0	383.38				−3.45	2.11	6	1	80.15
Paroxetine	40	mg	Tablets	Oral	5.4	0.03	2	329.37	−1.79		1.19	−1.97	4.24	4	1	41.89
Pefloxacin	400	mg	Tablets	Oral	11.4	0.1	12	333.37	−1.47	0.27	0.15	−0.61	−0.32	6	1	61.72
Pentamidine	300	mg	Powder	Injection (i.v.)	100	0.01	12	340.43	−0.53		−1.01	2.44	2.31	6	4	120.17
Pentoxifylline	400	mg	Tablets	Oral	191	0.008	0	278.31	−0.16	0.29	0.29	−2.98	0.12	4	0	66.77
Perindopril erbumine	8	mg	Tablets	Oral			8	368.48			−0.06	−0.95	1.21	5	2	101.91
Phenobarbital	60	mg	Tablets	Oral	1	0.2	24	232.24	−2.37	1.47	1.34	−2.62	1.37	3	2	83.96
Phenylbutazone	100	mg	Tablets	Oral	0.7	0.6	1	308.38	−2.64	3.16	0.73	−3.67	3.39	2	0	41.56
Phenylephrine hydrochloride	1	mg/mL	Solution (with promethazine HCl)	Injection (i.v.)				167.21		−0.31	−1.89	0.51	−0.09	2	0	60.00
Pimozide	2	mg	Tablets	Oral	0.008	1.0		461.56	−4.76	6.30	4.09	−5.02	6.40	2	1	33.99
Pramlintide acetate	0.6	mg/mL	Solution	Injection (s.c.)				3950.46				−17.83		60	56	1855.80
Prazosin	5	mg	Tablets	Oral	1.4	0.01	0.5	383.41	−2.44		0.79	−3.62	2.03	7	1	96.10
Prednisolone	5	mg	Tablets	Oral	0.38	0.05	16	360.45	−2.98	1.62	1.62	−3.68	1.42	5	3	104.22
Primaquine	15	mg	Tablets	Oral			1	259.35			−0.07	0.32	2.60	4	2	61.59
Prochlorperazine	10	mg	Tablets	Oral	0.1	0.4	0.1	373.95	−3.57	4.88	2.98	−4.05	4.38	3	0	2.92
Proguanil	100	mg	Tablets	Oral	9.09	0.04		253.74	−1.45	2.53		0.28	2.53	5	5	89.44
Promazine	100	mg	Tablets	Oral	333.33	0.001	2	284.43	0.07	4.55	2.52	−2.04	4.40	2	0	1.75
Promethazine	50	mg	Tablets	Oral			2	284.43		4.81	2.64	−2.21	4.40	2	0	1.75
Propantheline bromide	15	mg	Tablets	Oral	50	0.001	3.5	368.50	−0.87	−1.07	−1.07	−4.17	1.49	1	0	36.48

Table I. (Continued)

Generic name	Maximum strength dose value	Maximum strength dose unit	Formulation	Route	Measured solubility (mg/mL)	Dose number	% Excreted unchanged in urine	MW drug	Measured Log*S* molar	Measured Log*P*	Measured LogD_{74}	minVSLgS 3–7.5	CLog*P*	HBA	HBD	PSA
Propranolol hydrochloride	80	mg	Tablets	Oral	50	0.006	0.25	259.35	−0.71	3.48	1.20	−1.11	2.75	3	2	46.24
Propylthiouracil	50	mg	Tablets	Oral	1.2	0.2		170.23	−2.15		1.09	−1.83	0.97	1	2	46.21
Protriptyline	10	mg	Tablets	Oral	50	0.0008	1	263.39	−0.72		1.36	−1.10	4.87	1	1	14.57
Pyrazinamide	500	mg	Tablets	Oral	15	0.1	1.6	123.12	−0.91	−0.60	−0.59	−0.57	−0.68	3	1	66.73
Quetiapine fumarate	300	mg	Tablets	Oral	94	0.01	0.5	383.52	−0.97			−3.69	2.99	5	1	43.01
Quinacrine; mepacrine	100	mg	Tablets	Oral	28.57	0.01		399.97	−1.15		1.91	−2.09	6.72	4	1	34.79
Quinidine sulfate dihydrate	300	mg	Tablets	Oral	11.1	0.1	18	324.43	−1.85	3.44	1.82	−2.67	2.79	4	1	43.08
Quinine bisulfate heptahydrate	260	mg	Capsules	Oral	111.1	0.009	12	324.43	−0.69	3.44	1.82	−2.85	2.79	4	1	43.08
Rabeprazole sodium	20	mg	Capsules	Oral			0	359.45				−3.73	2.08	5	1	70.73
Ramelteon	8	mg	Tablets	Oral			0.1	259.35				−3.49	2.49	2	1	41.95
Ramipril	10	mg	Capsules	Oral			1.5	416.52			1.76	−1.27	1.54	5	2	101.91
Reboxetine	6	mg	Tablets	Oral	8	0.003	10	313.40	−1.59			−2.11	3.26	4	1	41.58
Remifentanil hydrochloride	1	mg/mL	Solution	Injection (i.v.)			0.1	376.46		1.85	1.25	−3.15	1.96	4	0	74.45
Reserpine	0.25	mg	Tablets	Oral	0.01	0.1	1	608.69	−4.78	3.72	4.14	−5.80	3.86	8	1	114.49
Ribavirin	200	mg	Tablets	Oral	142	0.006	17	244.21	−0.24	−1.85	−2.43	−0.90	−2.85	7	4	146.67
Ridogrel	5	mg	Tablets	Oral	0.02	1.0		366.34	−4.26			−3.58	4.54	5	1	72.68
Riluzole	50	mg	Tablets	Oral			2	234.20				−2.72	3.24	3	1	47.02
Rimantadine hydrochloride	100	mg	Tablets	Oral	50	0.008	20	179.31	−0.55		0.08	1.85	3.96	1	1	27.97
Risperidone	4	mg	Tablets	Oral	0.25	0.06	3	410.50	−3.22	3.04	2.52	−3.49	2.71	4	0	53.60
Rivastigmine	6	mg	Capsules	Oral			0.1	250.34				−1.56	2.10	2	0	29.73
Rizatriptan	10	mg	Tablets	Oral	42	0.0010	14	269.35	−0.81			−1.19	0.99	3	1	39.11
Ropinirole	5	mg	Tablets	Oral	133	0.0002	5	260.38	−0.29	2.70		−0.33	2.80	2	1	33.72
Ropivacaine	10	mg/mL	Solution	Injection (epidural)	53.8		1	274.41	−0.71	2.90	1.15	−3.25	3.16	2	1	33.72
Rosiglitazone maleate	8	mg	Tablets	Oral	0.04	0.8	0	357.43	−3.95			−3.80	3.02	5	1	71.34
Rotigotine	18	mg	Transdermal	Topical (skin. membranes)	5.6	0.01	0	315.48	−1.75	4.03	3.40	−2.44	4.54	2	1	24.05
Roxatidine acetate HCl	150	mg	Tablets	Oral			2	384.90			−0.55	−2.62	2.80	4	1	70.19
Salicylic acid	300	mg	Tablets	Oral	2.51	0.5	15	138.12	−1.74	2.26	−1.51	0.20	2.19	3	2	63.70
Scopolamine	10	mg	Tablets	Oral	666.67	0.00006	6	303.36	0.34	0.98	0.62	−1.72	0.29	4	1	59.59
Secobarbital (quinalbarbitone)	100	mg	Tablets	Oral	1.1	0.4		238.29	−2.34	1.97	1.97	−2.94	2.16	3	2	83.96
Selegiline; (−)-deprenil	5	mg	Tablets	Oral			0.1	187.29		2.90	2.67	−2.32	3.02	1	0	1.18
Sertraline hydrochloride	100	mg	Tablets	Oral	3.8	0.1	0.2	306.24	−1.91		2.74	−2.99	5.35	1	1	14.57
Sibutramine	15	mg	Capsules	Oral	2.9	0.02	0	279.86	−1.98	1.49		−2.19	5.59	1	0	1.18
Sildenafil	100	mg	Tablets	Oral	3.5	0.1	7.5	474.59	−2.13			−4.17	1.98	7	1	105.18
Solifenacin succinate	10	mg	Tablets	Oral			12.5	362.48				−3.16	4.68	2	0	29.42
Sparfloxacin	200	mg	Tablets	Oral	1.1	0.7	10	392.41	−2.55			−0.67	−0.61	7	3	102.79
Sufentanil	0.05	mg/mL	Solution	Injection (i.v.)			6	386.56		3.95	3.24	−3.23	3.59	3	0	29.11
Sumatriptan succinate	100	mg	Tablets	Oral	21.4	0.02	22	295.41	−1.14	0.93	−1.17	−0.96	0.74	3	2	67.24
Sunitinib malate	50	mg	Capsules	Oral	25	0.008	4	398.48	−1.20		5.40	−2.58	3.00	3	3	80.53
Tacrine	40	mg	Capsules	Oral			0.5	198.27		2.71	0.46	−0.12	3.27	2	1	37.91
Tamoxifen	20	mg	Tablets	Oral	0.5	0.2	0.5	371.53	−2.87		6.56	−4.42	6.82	2	0	10.28
Tamsulosin	0.4	mg	Capsules	Oral			8.7	408.52				−2.96	2.17	6	2	107.38
Temazepam	30	mg	Capsules	Oral	0.604	0.2	0.5	300.75	−2.70	2.19	1.79	−3.58	2.34	3	1	51.32
Temocapril	4	mg	Tablets	Oral			1.5	476.62				−1.98	2.10	5	2	101.91
Temsirolimus	10	mg/mL	Solution	Injection (i.v.)	0.01		4.6	1030.31	−5.01			−9.52	0.67	14	4	253.80
Tenoxicam	20	mg	Tablets	Oral	0.803	0.10	0.1	337.38	−2.62		−0.32	−0.17	1.61	5	2	104.05
Terazosin	10	mg	Tablets	Oral	24.2	0.002	10	387.44	−1.20		−4.64	−3.71	2.18	8	1	95.48
Theophylline	600	mg	Tablets	Oral	8.3	0.3	18	180.17	−1.34	−0.04	−0.02	−1.87	−0.03	3	1	61.90
Thioguanine	40	mg	Tablets	Oral	0.2	0.8	0.5	167.19	−2.92			−0.79	−1.70	3	3	76.09
Thiopental	1000	mg	Powder	Injection (i.v.)	50	0.08	0.5	242.34	−0.69	2.85	2.84	−3.26	2.98	2	2	65.69

Thioridazine	200	mg	Tablets	Oral	1	0.8		370.58	−2.57	5.90	3.55	−3.53	6.00	2	0	1.75
Ticlopidine	250	mg	Tablets	Oral			0.5	263.79			3.37	−3.48	4.39	1	0	1.18
Tilidine; tilidate	50	mg	Capsules	Oral			0.1	273.38				−2.77	3.76	2	0	28.24
Timolol	20	mg	Tablets	Oral	2.74	0.03	15	316.43	−2.06	1.83	1.91	−0.74	1.21	7	2	75.98
Tinidazole	500	mg	Tablets	Oral	20	0.1	22.5	247.27	−1.09	−0.35	−0.33	−1.71	−0.32	5	0	91.72
Tolterodine	2	mg	Tablets	Oral	12	0.0007	1	325.50	−1.43			−2.28	5.24	2	1	24.05
Toremifene	60	mg	Tablets	Oral	0.38	0.6	0.1	405.97	−3.03			−4.75	6.53	2	0	10.28
Tramadol	50	mg	Tablets	Oral			20	263.38		2.63		−0.59	3.10	3	1	32.84
Tranylcypromine sulfate	10	mg	Tablets	Oral	48	0.0008		133.19	−0.44		0.69	−0.33	1.48	1	1	27.97
Triamcinolone	4	mg	Tablets	Oral	0.08	0.2	1	394.44	−3.69	1.16	1.16	−3.07	0.71	6	4	126.78
Triamcinolone acetonide	4	mg	Tablets	Oral	0.114	0.1	1	434.51	−3.58	2.53	2.30	−4.17	2.21	6	2	99.25
Triazolam	0.5	mg	Tablets	Oral	0.045	0.04	2	343.22	−3.88	2.42	1.63	−4.21	2.62	3	0	33.27
Trifluoperazine	10	mg	Tablets	Oral	50	0.0008		407.50	−0.91	5.03	3.14	−3.80	4.69	3	0	2.92
Trihexyphenidyl (benzhexol)	5	mg	Tablets	Oral	10	0.002		301.48	−1.48	4.82		−1.94	5.15	2	1	23.73
Trimetrexate glucuronate	200	mg	Powder	Injection (i.v.)	50	0.02	20	369.43	−0.87	1.63		−3.54	1.84	8	3	117.41
Tropisetron	5	mg	Capsules	Oral	11	0.002	8	284.36	−1.41		0.65	−1.94	2.88	2	1	42.21
Urapidil	5	mg/mL	Solution	Injection (i.v.)	19		15	387.49	−1.31	1.60	2.02	−3.74	2.44	6	1	63.11
Valacyclovir	1000	mg	Caplets	Oral	174	0.02	0.5	324.34	−0.27			−1.59	−1.22	7	3	144.80
Valganciclovir; valcyte	450	mg	Tablets	Oral	70	0.03		354.37	−0.70		−2.05	−1.54	−2.18	9	4	167.36
Valproic acid	250	mg	Tablets	Oral	1.3	0.8	1.8	144.22	−2.05	2.75	0.13	−1.45	2.76	2	1	40.83
Vardenafil	20	mg	Tablets	Oral	0.11	0.7	4	488.61	−3.65			−4.03	2.23	7	1	104.88
Vasopressin	60.8	μg/mL	Solution (20 units per mL)	Injection (s.c.)	0.1		5	1084.25	−4.04			−2.25	−3.82	16	15	504.48
Venlafaxine hydrochloride	150	mg	Tablets	Oral	572	0.001	4.6	277.41	0.31			−1.52	3.27	3	1	32.84
Verapamil hydrochloride	120	mg	Tablets	Oral	0.75	0.64	1.5	454.61	−3.05	3.79		−4.11	4.47	6	0	56.29
Vinblastine	1	mg/mL	Solution	Injection (i.v.)	10		0.5	811.00	−1.91	3.70	3.69	−6.97	5.23	9	3	152.61
Vincristine	1	mg/mL	Solution	Injection (i.v.)	10		15	824.98	−1.92		2.57	−6.35	4.04	9	3	170.88
Vinorelbine tartrate	10	mg/mL	Solution	Injection (i.v.)	1000		11	778.95	0.11			−6.71	5.94	8	2	130.05
Vitamin B6 (pyridoxine)	25	mg	Capsules	Oral	222	0.0005		169.18	0.12	−0.77		−0.75	−0.35	4	3	78.23
Vitamin D3 (cholecalciferol)	1.4	mg	Tablets	Oral	0.1	0.06		384.65	−3.59			−6.71	9.48	1	1	22.56
Vorozole	2.5	mg	Tablets	Oral			8	324.78				−4.16	2.20	4	0	50.83
Zidovudine	300	mg	Capsules	Oral	25	0.05	2.8	267.25	−1.03	0.05	0.08	−2.31	0.04	6	2	127.30
Zolmitriptan	5	mg	Tablets	Oral	20	0.001	8	287.36	−1.16			−1.03	1.29	2	2	56.78
Zolpidem tartrate	10	mg	Tablets	Oral	23	0.002	0.5	307.40	−1.13		2.35	−4.20	3.03	3	0	29.96
Zonisamide	100	mg	Capsules	Oral	0.8	0.5	22	212.23	−2.42		−0.10	−1.30	−0.36	3	1	88.84
Zopiclone	7.5	mg	Tablets	Oral	0.12	0.3	4.5	388.82	−3.51	1.50	−0.90	−2.84	1.25	6	0	79.29

Table II. Measured and *In Silico* Data for 265 BDDCS Class 2 Drugs

Generic name	Maximum strength dose value	Maximum strength dose unit	Formulation	Route	Measured solubility (mg/mL)	Dose number	% Excreted unchanged in urine	MW drug	Measured LogS molar	Measured LogP	Measured LogD74	minVSLgS 3–7.5	CLogP	HBA	HBD	PSA
10-Hydroxy-carbamazepine		Active metabolite			0.045		27	254.29	−3.75		1.26	−3.15	1.21	2	2	32.78
6-Methoxy-2-naphthyl-acetic acid		Active metabolite					1	216.24			−0.30	−2.29	2.51	3	1	49.94
Acitretin	25	mg	Capsules	Oral			0	326.44		6.40		−5.07	6.07	3	1	49.94
Adapalene	6	mg	Cream, gel, solution	Topical (skin. membranes)				412.53		7.88		−5.78	9.15	3	1	49.94
Albendazole	200	mg	Tablets	Oral			0	265.34			2.85	−3.54	3.46	3	2	65.55
Albendazole sulfoxide		Active metabolite					1	281.34				−3.28	3.46	3	2	65.55
Allopurinol	300	mg	Tablets	Oral	0.569	2.1	12	136.11	−2.38	−0.55	−0.55	−1.18	0.63	3	2	70.47
Altretamine	50	mg	Capsules	Oral			0.5	210.28		2.73		−3.02	1.67	6	0	33.35
Aminoglutethimide	250	mg	Tablets	Oral				232.28			1.41	−2.35	0.77	3	2	78.79
Amiodarone hydrochloride	400	mg	Tablets	Oral	0.7	2.3	0	645.32	−2.96	7.80	2.54	−5.40	8.95	3	0	37.97
Amphotericin B	2	mg/mL	Solution	Injection (i.v.)	0.1		3.5	924.10	−3.97			−6.40	−3.65	17	12	347.83
Amprenavir	50	mg	Capsules	Oral	0.04	5.0	1	505.64	−4.10			−5.03	3.29	6	3	139.36
Anidulafungin	3.33	mg/mL	Solution	Injection (i.v.)	0.05		0.5	1140.27	−4.36			−10.68	2.20	17	14	415.56
Aprepitant	125	mg	Capsules	Oral			0	534.44				−5.28	4.60	5	2	78.12
Argatroban	1	mg/mL	Solution	Injection (i.v.)			16	508.64				−1.80	−0.57	9	6	192.20
Aripiprazole	30	mg	Tablets	Oral	0.0001	1200	0.5	448.40	−6.65		3.20	−4.64	5.31	4	1	43.70
Armodafinil	250	mg	Tablets	Oral			8	273.36				−2.82	0.94	2	1	64.62
Artemether	50	mg	Tablets	Oral				298.38				−3.35	3.05	5	0	49.50
Astemizole	10	mg	Tablets	Oral			0.5	458.58		5.70	3.88	−5.40	6.09	4	1	35.37
Atazanavir sulfate	300	mg	Capsules	Oral			7	704.87				−7.38	5.92	7	5	186.22
Atorvastatin calcium	80	mg	Tablets	Oral	0.0000204	15686	1	558.66	−7.44			−6.47	4.46	5	4	119.06
Azelastine hydrochloride	457	μg/mL	Solution	Ophthalmic			2	381.91			1.96	−2.37	4.01	3	0	33.17
Bevantolol	200	mg	Tablets	Oral	0.1843	4.3	8	345.44	−3.27	3.00	3.00	−3.15	3.00	5	2	64.45
Bexarotene	75	mg	Capsules	Oral			0.01	348.49				−4.74	8.19	2	1	40.83
Bezafibrate	200	mg	Capsules	Oral			40	361.83			−0.17	−3.79	3.70	4	2	82.78
Bicalutamide	50	mg	Tablets	Oral	0.005	40		430.38	−4.93			−4.32	2.71	5	2	110.56
Bosentan	125	mg	Tablets	Oral	0.001	500	2	551.63	−5.74			−5.38	4.17	9	2	142.96
Buspirone	10	mg	Tablets	Oral	0.0214	1.9	0.1	385.51	−4.26	2.63	3.39	−3.50	2.19	6	0	60.25
Cabergoline	0.5	mg	Tablets	Oral			3	451.62				−4.28	4.77	4	2	118.24
Calcipotriene; calcipotriol	0.05	μg/mL	Solution	Topical (skin, membranes)			0.5	412.62				−5.58	5.27	3	3	67.68
Calcitriol	0.5	μg	Capsules	Oral			8	416.65				−6.35	6.04	3	3	67.68
Capsaicin	179	mg	Cream	Topical	0.06	12	0	305.42	−3.71			−4.49	4.00	3	2	64.82
Carbamazepine	300	mg	Tablets	Oral	0.256	4.7	0.5	236.28	−2.97	2.45	2.45	−3.32	2.38	1	1	46.81
Carbamazepine 10,11-epoxide		Active metabolite			0.1		0.5	252.28	−3.40	0.69	0.69	−3.00	0.24	1	1	55.61
Carvedilol	25	mg	Tablets	Oral	0.01	10	1	406.49	−4.61	4.19		−4.30	4.04	5	3	78.42
Cefditoren pivoxil	200	mg	Tablets	Oral	0.08	10	5	620.73	−3.89			−6.88	2.71	9	2	176.19
Cefpodoxime proxetil	200	mg	Tablets	Oral	0.3	2.7	0	557.61	−3.27			−4.79	0.80	10	2	183.53
Celecoxib	200	mg	Capsules	Oral	0.005	160	2	381.38	−4.88			−4.47	4.37	3	1	78.91
Chlorzoxazone	500	mg	Tablets	Oral	0.25	8.0	0.5	169.57	−2.83			−1.77	2.51	2	1	42.53
Ciclesonide	0.16	mg/inhalation	Solution	Topical (nasal)	0.0002	3.2	0	540.70	−6.43			−6.25	5.25	6	1	103.75
Cilostazol	100	mg	Tablets	Oral	0.003	133		369.47	−5.09			−4.87	3.53	5	1	81.66
Cinacalcet	90	mg	Tablets	Oral	0.1	3.6	0.1	357.42	−3.55			−3.12	6.35	1	1	14.57
Cisapride	20	mg	Tablets	Oral	0.0027	30		465.96	−5.24		3.39	−4.57	3.81	6	2	88.69
Citalopram	40	mg	Tablets	Oral	0.031	5.2	12	324.40	−4.02	3.41	0.74	−2.83	3.13	3	0	28.67
Cladribine	1	mg/mL	Solution	Injection (i.v.)			18	285.69		0.02	0.24	−2.15	−0.91	7	3	112.88
Clofazimine	50	mg	Capsules	Oral	0.001	200	0.2	473.41	−5.68	7.48		−5.84	7.70	4	1	34.09
Clofibrate	500	mg	Capsules	Oral			11	242.70		3.60	3.60	−1.63	3.02	3	1	36.17
Clopidogrel bisulfate	75	mg	Tablets	Oral	0.05078	5.9		321.83	−3.80			−3.83	4.21	2	0	28.24
Clotrimazole	10	mg	Tablets	Oral	0.003	13	5	344.85	−5.06	4.80		−5.07	5.25	1	0	10.81
Clozapine	100	mg	Tablets	Oral	0.0118	34	0.5	326.83	−4.44	3.23	2.99	−4.37	3.71	4	1	25.63

Conivaptan hydrochloride	5	mg/ml	Solution	Injection (i.v.)	0.15		1	498.59	−3.55			−6.73	5.00	3	2	75.90
Cyclosporine	100	mg	Capsules	Oral	0.008	50	0.1	1202.64	−5.18	2.95	2.92	−10.73	14.36	12	5	290.07
Cyproterone acetate	50	mg	Tablets	Oral	0.0021	95	1	416.95	−5.30			−4.83	3.96	3	0	63.61
Danazol	200	mg	Capsules	Oral	0.0009	889		337.47	−5.57			−4.54	3.93	2	1	45.90
Dapsone	100	mg	Tablets	Oral	0.2	2.0	15	248.31	−3.09	0.97	0.97	−2.71	0.89	4	2	92.10
Darunavir	600	mg	Capsules	Oral	0.15	16	1.2	547.68	−3.56			−5.44	2.89	7	3	148.15
Dasatinib	70	mg	Tablets	Oral			0.1	488.02				−4.70	2.88	8	3	101.85
Daunorubicin	5	mg/mL	Solution	Injection (i.v.)	0.0392		0.5	527.53	−4.13	1.83	1.83	−3.89	0.84	11	5	200.34
Delavirdine	200	mg	Caplets	Oral	0.00081	988	2.5	456.57	−5.75			−4.80	2.41	6	3	110.60
Desloratadine	5	mg	Tablets	Oral	0.000077	260	5	310.83	−6.61			−2.42	3.83	2	1	24.82
Diazoxide	100	mg	Capsules	Oral	0.15	2.7	35	230.67	−3.19	1.81	1.08	−2.00	1.42	3	1	61.41
Dicoumarol	100	mg	Tablets	Oral	0.128	3.1	0.5	336.30	−3.42	2.07	1.86	−3.06	3.66	4	2	101.12
Diflunisal	500	mg	Tablets	Oral			6	250.20		4.44	0.76	−2.17	4.40	3	2	63.70
Diloxanide furoate	500	mg	Tablets	Oral			1	328.15		1.96		−4.03	3.09	2	0	55.94
Dipyridamole	75	mg	Tablets	Oral	0.007	43	0.1	504.64	−4.86		3.71	−4.21	1.49	12	4	134.70
Disulfiram	250	mg	Tablets	Oral	0.2	5.0	0	296.54	−3.17	3.88	3.88	−4.19	3.88	0	0	2.35
Docetaxel	40	mg/mL	Solution	Injection (i.v.)	0.0065		5	807.90	−5.09			−7.05	4.08	10	5	240.13
Domperidone	20	mg	Tablets	Oral	0.006	13	0	425.92	−4.85	3.90	3.33	−4.31	4.27	3	2	66.80
Donepezil	10	mg	Tablets	Oral	0.0029	14	10.6	379.50	−5.12			−4.10	4.60	4	0	37.66
Dronabinol; tetrahydrocannabinol	10	mg	Capsules	Oral			0.5	314.47		6.97	3.78	−5.91	7.24	2	1	31.98
Dronedarone	400	mg	Tablets	Oral	0.5	3.2	0	556.77	−3.05			−4.24	8.57	5	1	89.77
Drospirenone	3	mg	Tablets	Oral			0.1	366.50				−4.11	2.84	2	0	45.34
Dutasteride	0.5	mg	Capsules	Oral			0.5	528.54				−6.05	4.94	2	2	65.39
Ebastine	10	mg	Tablets	Oral			2	469.67			2.78	−5.87	6.94	3	0	28.24
Efavirenz	600	mg	Capsules	Oral	0.005	480	0.5	315.68	−4.80			−3.99	4.67	2	1	41.34
Entacapone	200	mg	Tablets	Oral	0.0166	48	0.2	305.29	−4.26			−2.73	1.76	6	2	128.04
Eplerenone	50	mg	Tablets	Oral			3	414.50			0.85	−4.02	0.29	4	0	81.19
Erlotinib hydrochloride	163.9	mg	Tablets	Oral	0.4	1.6	0.3	393.45	−2.99			−5.20	4.34	7	1	70.25
Estazolam	2	mg	Tablets	Oral	0.0015	5.3	4	294.75	−5.29			−3.73	2.29	3	0	33.27
Ethchlorvynol	750	mg	Capsules	Oral			0.05	144.60			2.06	−2.16	1.57	1	1	22.56
Etizolam	1	mg	Tablets	Oral			0.3	342.85				−3.82	2.87	3	0	33.27
Etodolac	600	mg	Tablets	Oral	0.01	240	1	287.36	−4.46	3.81	1.14	−2.81	3.43	3	2	63.59
Etomidate	2	mg/mL	Solution	Injection (i.v.)	0.045		2	244.30	−3.73	3.05	3.05	−3.49	2.67	2	0	37.88
Etoricoxib; arcoxia	120	mg	Tablets	Oral	0.14	3.4	0.5	358.85	−3.41			−4.52	2.35	4	0	57.25
Etravirine	100	mg	Tablets	Oral			0	435.29				−6.76	5.22	6	2	108.94
Exemestane	25	mg	Tablets	Oral			1	296.41				−3.95	3.28	2	0	36.54
Ezetimibe	10	mg	Tablets	Oral			2	409.44				−5.56	3.96	3	2	64.57
Febuxostat	80	mg	Tablets	Oral	0.013	25	3	316.38	−4.39			−3.59	4.40	5	1	78.88
Felodipine	10	mg	Tablets	Oral	0.001	40	0.25	384.26	−5.58	3.86		−4.73	5.30	3	1	68.70
Fenofibrate	145	mg	Capsules	Oral	0.0008	725	0.1	360.84	−5.65		4.80	−5.47	5.23	3	0	54.44
Flufenamic acid	100	mg	Tablets	Oral	0.0265	15	7	281.24	−4.03	5.25	2.06	−3.41	5.53	3	2	54.80
Flunarizine	10	mg	Tablets	Oral	0.0165	2.4	0.2	404.51	−4.39	5.78	4.90	−5.69	6.34	2	0	2.35
Fluphenazine hydrochloride	10	mg	Tablets	Oral	0.031	1.3	0.1	437.53	−4.22		3.48	−4.11	4.12	4	1	25.48
Flurbiprofen	100	mg	Capsules	Oral			2.9	244.27		4.16	0.91	−2.76	3.75	2	1	40.83
Flutamide	125	mg	Capsules	Oral	0.0095	53	0.5	276.22	−4.46	3.35	4.06	−3.17	3.34	3	1	76.69
Fluticasone propionate	50	μg/inhalation	Suspension	Topical (nasal)	0.00051	3.9	3	500.58	−5.99			−4.82	3.80	4	1	86.17
Folic acid	5	mg	Tablets	Oral	0.0016	13		441.41	−5.44	−0.52		−2.59	−2.31	12	6	219.42
Fosamprenavir calcium	700	mg	Capsules	Oral	0.31	9.0	0	585.62	−3.28			−0.53	3.04	8	4	189.86
Fosinopril	40	mg	Tablets	Oral	0.022	7.3	0	563.68	−4.41		2.32	−5.95	7.45	5	1	115.00
Fulvestrant	50	mg/mL	Solution	Injection (i.m.)	0.001	200	0.1	606.79	−5.78			−8.28	7.35	3	2	63.81
Gefitinib	250	mg	Tablets	Oral	0.0017	588	2	446.91	−5.42	4.85		−4.77	5.60	7	1	62.63
Gemfibrozil	600	mg	Tablets	Oral	0.019	126	0.5	250.34	−4.12		1.33	−3.15	3.94	3	1	49.94
Gliclazide	80	mg	Tablets	Oral	0.0039	82	0.5	323.42	−4.92	1.36	−0.07	−2.98	1.09	4	2	89.39
Glimepiride	4	mg	Tablets	Oral	0.0012	13	0	490.63	−5.61			−5.70	3.96	5	3	137.24
Glipizide	10	mg	Tablets	Oral			4.5	445.54		1.91	−0.40	−4.49	2.57	6	3	138.28
Glyburide; glibenclamide	6	mg	Tablets	Oral	0.004	6.0	0	494.01	−5.09		1.41	−5.47	4.24	5	3	126.89
Griseofulvin	500	mg	Tablets	Oral			0.3	352.77		2.18	2.18	−3.19	1.91	6	0	72.65
Haloperidol	20	mg	Tablets	Oral	0.037	2.2	1	375.87	−4.01	4.30	3.16	−3.68	3.85	3	1	42.01
Ibuprofen	800	mg	Capsules	Oral	0.038	84	0.5	206.29	−3.73	3.97	0.81	−2.31	3.68	2	1	40.83
Idebenone	180	mg	Capsules	Oral			0.5	338.45				−4.81	3.42	5	1	76.69

Table II. (Continued)

Generic name	Maximum strength dose value	Maximum strength dose unit	Formulation	Route	Measured solubility (mg/mL)	Dose number	% Excreted unchanged in urine	MW drug	Measured LogS molar	Measured LogP	Measured LogD74	minVSLgS 3–7.5	CLogP	HBA	HBD	PSA
Iloperidone	12	mg	Tablets	Oral	0.03	1.6	0.5	426.49	−4.15			−3.87	4.27	5	0	61.00
Imatinib mesylate	400	mg	Capsules	Oral	1	1.6	5	493.62	−2.69			−5.77	4.53	7	2	79.59
Indinavir sulfate	400	mg	Capsules	Oral	0.015	107		613.81	−4.61	2.92		−6.21	3.68	7	4	123.40
Indobufen	200	mg	Tablets	Oral			13	295.34			−0.70	−3.20	3.27	3	1	59.98
Indomethacin	50	mg	Tablets	Oral	0.0025	80	15	357.80	−5.16	4.27	0.77	−3.93	4.18	4	1	68.78
Indoramin	25	mg	Tablets	Oral			5	347.46		3.23	2.29	−3.86	2.84	2	2	47.99
Irbesartan	300	mg	Tablets	Oral	0.08	15	2.5	428.54	−3.73		1.00	−2.82	6.04	5	1	82.47
Isotretinoin; 13-*cis*-retinoic acid	40	mg	Capsules	Oral			0.5	300.44		6.30	4.23	−4.80	6.74	2	1	40.83
Isradipine	5	mg	Capsules	Oral	0.008	2.5	0	371.40	−4.67	4.28	3.67	−4.14	3.92	5	1	105.96
Itraconazole	100	mg	Capsules	Oral	0.000001	400000	0.03	705.65	−8.85	5.66	3.27	−8.44	5.99	9	0	84.66
Ixabepilone	1.915	mg/mL	Solution	Injection (i.v.)			5.6	506.71				−5.51	3.08	6	3	115.27
Ketanserin	40	mg	Tablets	Oral	0.05	3.2	0.5	395.44	−3.90	3.29	2.18	−5.10	3.00	4	1	70.53
Ketoconazole	200	mg	Tablets	Oral	0.0069	116	3	531.44	−4.89	4.35	4.05	−5.99	3.64	6	0	57.83
Ketoprofen	75	mg	Capsules	Oral	0.18	1.7	0.5	254.29	−3.15	3.12	−0.01	−2.82	2.76	3	1	59.10
Lamotrigine	200	mg	Tablets	Oral	0.17	4.7	10	256.10	−3.18		−0.19	−2.75	2.53	5	2	88.97
Lansoprazole	30	mg	Capsules	Oral	0.00097	124	0	369.37	−5.58		2.36	−3.74	2.60	4	1	61.94
Lapatinib ditosylate	250	mg	Tablets	Oral	0.001	1000	1	581.07	−5.76			−7.19	5.97	7	2	104.31
Latanoprost	0.5	mg/mL	Solution	Ophthalmic	0.05			432.61	−3.94			−6.14	3.60	4	3	94.74
Leflunomide	100	mg	Tablets	Oral	0.023	17	1	270.21	−4.07			−2.99	2.32	2	1	55.88
Lofepramine	70	mg	Tablets	Oral			4	418.97			6.57	−6.58	7.29	3	0	20.02
Lopinavir	200	mg	Capsules (with 50 mg ritonavir)	Oral			2.2	628.82				−7.32	6.10	5	4	131.37
Loratadine	10	mg	Tablets	Oral	0.005	8.0	5	382.89	−4.88	5.20	5.20	−5.32	5.05	2	0	38.48
Losartan potassium	100	mg	Tablets	Oral	0.048	8.3	12	422.92	−3.98			−2.04	4.10	5	2	86.79
Lovastatin	40	mg	Tablets	Oral	0.0004	400	10	404.55	−6.00	4.26	4.26	−4.95	4.08	3	1	76.69
Mebendazole	100	mg	Tablets	Oral				295.30		2.83	2.42	−4.00	3.08	4	2	83.82
Mefenamic acid	250	mg	Tablets	Oral	0.08	13	1	241.29	−3.48	5.12		−3.36	5.29	3	2	54.80
Mefloquine	250	mg	Tablets	Oral			9	378.32			0.72	−3.12	3.67	3	2	47.38
Meloxicam	15	mg	Tablets	Oral	0.012	5.0	0.2	351.41	−4.47	3.02	0.10	−2.15	2.29	5	2	104.05
Mercaptopurine; 6-mercaptopurine	50	mg	Tablets	Oral			22	152.18		0.01	0.39	1.74	0.82	3	2	44.70
Mesalamine; mesalazine	1200	mg	Tablets	Oral	1	4.8	7	153.14	−2.19		−3.20	1.97	1.06	4	3	91.37
Metaxalone	800	mg	Tablets	Oral	0.3	11	2	221.26	−2.87	2.42		−2.49	2.15	2	1	50.74
Methaqualone	500	mg	Tablets	Oral	0.3	6.7	0.2	250.30	−2.92	2.50	2.50	−3.83	3.65	2	0	28.78
Miconazole	1200	mg	Cream, suppository	Topical (skin, membranes)	0.89	5.4	0	416.14	−2.67	5.34	6.34	−5.83	5.81	2	0	19.61
Mizolastine	10	mg	Tablets	Oral	0.013	3.1	5	432.50	−4.52			−5.28	2.84	5	1	55.05
Modafinil	200	mg	Tablets	Oral			8	273.36				−2.92	0.94	2	1	64.62
Mometasone furoate	200	µg/activation	Powder	Topical (aerosol)			0.5	521.44				−5.87	4.12	4	1	89.90
Montelukast sodium	10	mg	Tablets	Oral			0.2	586.20				−7.75	8.47	4	2	73.63
Mycophenolate		Active metabolite					0.5	320.35			0.20	−3.44	2.29	5	2	99.87
Mycophenolate mofetil	500	mg	Tablets	Oral	0.043	47	0	433.51	−4.00		2.37	−4.67	2.98	6	1	96.07
Nabumetone	750	mg	Tablets	Oral	0.015	200	0	228.29	−4.18	3.08	3.38	−3.51	2.98	2	0	27.38
Nalidixic acid	1000	mg	Tablets	Oral	0.054	74		232.24	−3.63	1.59	0.59	−1.88	1.02	5	1	69.92
Naproxen	500	mg	Tablets	Oral	0.115	17	0.5	230.27	−3.30	3.18	1.70	−2.50	2.82	3	1	49.94
Nateglinide	120	mg	Tablets	Oral	0.322	1.5	13	317.43	−2.99			−3.53	4.30	3	2	73.68
Nefazodone	100	mg	Tablets	Oral			0.1	470.02		5.00		−5.94	5.73	5	0	43.72
Nelarabine	5	mg/mL	Solution	Injection (i.v.)	1		6.6	297.27	−2.47			−1.56	−0.46	9	4	112.88
Nelfinavir	625	mg	Tablets	Oral				567.80				−6.89	5.84	5	4	112.29
Nevirapine	200	mg	Tablets	Oral	0.1	8.0		266.31	−3.43	1.81		−3.15	2.65	4	1	53.60
Nifedipine	20	mg	Capsules	Oral	0.006	13	0.01	346.34	−4.76	2.20	2.80	−3.66	3.13	5	1	112.85
Nifurtimox	250	mg	Tablets	Oral			1	287.30				−2.02	0.02	6	0	104.39

Nilotinib	200	mg	Capsules	Oral			4	529.53			−1.10	−7.56	5.84	6	2	87.75
Nilvadipine	2	mg	Tablets	Oral	0.0013	6.2	0	385.38	−5.47			−4.10	3.04	6	1	131.55
Nimesulide	100	mg	Tablets	Oral	0.014	29	2	308.31	−4.34	1.79		−3.01	3.21	4	1	105.36
Nimodipine	30	mg	Capsules	Oral	0.0025	48	0.5	418.45	−5.22	3.05	2.86	−4.68	4.00	6	1	121.64
Nitrazepam	10	mg	Capsules	Oral	0.0254	1.6	0.5	281.27	−4.04	2.25	2.16	−3.51	2.32	4	1	86.30
Nitrendipine	20	mg	Capsules	Oral	0.0022	36	0.5	360.37	−5.21	2.88		−4.20	3.73	5	1	112.85
Norelgestromin	6	mg	Tablets	Oral				327.47		2.70		−4.56	4.10	3	2	57.94
Norethindrone acetate	5	mg	Tablets	Oral	0.005	4.0	0	340.47	−4.83			−4.89	3.93	2	1	45.34
Olanzapine	40	mg	Tablets	Oral	0.01	16	7	312.44	−4.49	3.00		−3.79	3.01	4	1	25.63
Oxaprozin	600	mg	Tablets	Oral	1.7	1.4	0.5	293.33	−2.24	4.19	1.03	−3.58	2.95	3	1	60.49
Oxatomide	30	mg	Tablets	Oral	0.043	2.8	0	426.57	−4.00	5.42	3.39	−5.49	5.62	3	1	35.16
Oxazepam	30	mg	Tablets	Oral	0.045	2.7	0.5	286.72	−3.80	2.24	2.24	−3.55	2.31	3	2	64.71
Oxcarbazepine	600	mg	Tablets	Oral	0.085	28		252.28	−3.47		1.25	−3.18	1.21	2	1	65.09
Paclitaxel	6	mg/mL	Solution	Injection (i.v.)			5	853.93			6.83	−7.35	4.73	10	4	235.84
Paricalcitol	4	μg	Capsules	Oral			0	416.65				−6.29	5.69	3	3	67.68
Pentazocine	50	mg	Tablets	Oral	0.0449	4.5	15	285.43	−3.80	3.31	0.83	−2.06	4.67	2	1	24.05
Pergolide	1	mg	Tablets	Oral				314.50			3.97	−3.98	4.40	1	1	15.14
Perhexiline	100	mg	Tablets	Oral	0.00006	6667		277.50	−6.67		3.93	−1.41	7.15	1	1	14.57
Phenacetin	500	mg	Tablets	Oral	0.73	2.7		179.22	−2.39	1.58		−2.16	1.77	2	1	41.65
Phenytoin sodium	300	mg	Tablets	Oral	0.02	60	2	252.28	−4.14	2.47	2.47	−3.25	2.09	2	2	65.69
Pimecrolimus	10	mg/g	Cream	Topical (skin, membranes)			0	810.47				−8.00	5.30	10	2	163.34
Pioglitazone	45	mg	Tablets	Oral			0.5	356.45				−1.08	3.53	4	1	70.46
Piroxicam	20	mg	Capsules	Oral	0.0073	11	5	331.35	−4.66	3.06	0.20	−0.23	1.89	5	2	104.05
Pitavastatin	4	mg	Tablets	Oral				421.47			1.50	−1.51	3.59	5	3	96.19
Posaconazole	40	mg/mL	Suspension	Oral	0.00005		0.1	700.80	−7.15			−7.92	4.11	9	1	98.43
Prasugrel	10	mg	Tablets	Oral			1	373.45				−4.26	3.43	3	0	46.82
Prazepam	30	mg	Tablets	Oral	0.004	30	0	324.81	−4.91	3.73	3.73	−4.53	3.93	2	0	28.76
Praziquantel	600	mg	Tablets	Oral	0.4	6.0	2	312.42	−2.89		2.44	−3.89	3.36	2	0	38.89
Prednisone	50	mg	Tablets	Oral	0.133	1.5	3	358.44	−3.43	1.46	1.46	−3.57	1.66	5	2	99.93
Primidone	250	mg	Tablets	Oral	0.6	1.7	35	218.26	−2.56	0.91	−0.84	−2.59	0.88	2	2	65.69
Probenecid	500	mg	Tablets	Oral			1.2	285.36		3.21	−0.26	−2.36	3.37	4	1	79.53
Probucol	500	mg	Tablets	Oral				516.86			10.40	−8.32	10.97	2	2	45.74
Progesterone	200	mg	Capsules	Oral	0.007	114	0	314.47	−4.65	3.87		−4.25	3.78	2	0	36.54
Propafenone hydrochloride	300	mg	Tablets	Oral	0.093	13	0.5	341.45	−3.56			−2.21	3.64	4	2	64.51
Propofol	10	mg/mL	Emulsion	Injection (i.v.)	0.164		0.5	178.28	−3.04	3.79	4.16	−3.29	3.93	1	1	22.87
Propoxyphene napsylate	500	mg	Tablets	Oral	0.0196	102		367.54	−4.27			−0.95	5.32	2	1	41.64
Proscillaridin	0.5	mg	Capsules	Oral				530.66		2.48	2.48	−5.09	3.66	7	4	135.51
Pyrantel pamoate	180	mg	Caplet	Oral	0.5	1.4	7	206.31	−2.62			1.01	3.03	2	0	10.79
Quazepam	15	mg	Tablets	Oral				386.80		4.03	3.87	−4.62	3.20	1	0	10.48
Quinapril	40	mg	Tablets	Oral	0.001	160	3.1	438.53	−5.64		2.26	−1.82	1.74	5	2	101.91
Raloxifene; keoxifene	60	mg	Tablets	Oral	0.013	18	0.1	473.60	−4.56			−5.56	6.86	5	2	74.29
Raltegravir potassium	400	mg	Tablets	Oral			9	444.43			0.45	−3.79	1.16	7	3	150.45
Ranolazine	1000	mg	Tablets	Oral			6	427.55				−4.58	1.01	6	2	75.66
Repaglinide	2	mg	Tablets	Oral			1.5	452.60				−2.42	5.30	5	2	83.65
Rifabutin	150	mg	Capsules	Oral	0.19	3.2	10	847.03	−3.65	3.20		−5.36	4.73	13	5	216.49
Rifampin	300	mg	Capsules	Oral			7	822.96			1.32	−4.36	3.71	14	6	233.54
Ritonavir	100	mg	Capsules	Oral			3.5	720.96				−8.08	4.94	6	4	151.55
Rofecoxib	50	mg	Tablets	Oral	0.1	2.0	1	314.36	−3.50			−2.83	1.80	3	0	63.82
Romidepsin	5	mg/mL	Solution	Injection (i.v.)				540.71				−4.16	3.44	5	4	158.44
Rufinamide	400	mg	Tablets	Oral	0.059	27	1	238.20	−3.61			−2.26	0.51	3	1	73.11
Salmeterol xinafoate	0.05	mg	Powder	Topical (aerosol)			2.5	415.58				−3.01	3.06	5	4	91.35
Saquinavir methanesulfonate	500	mg	Capsules	Oral	0.08	25	2	670.86	−3.98	4.70		−6.91	4.73	7	5	178.75
Simvastatin	80	mg	Tablets	Oral	0.03	11	10	418.58	−4.14	4.68	4.68	−5.15	4.48	3	1	76.69
Sirolimus	2	mg	Tablets	Oral			2	914.20				−9.32	7.04	12	3	204.17
SN-38; 7-ethyl-10-hydroxycamptothecin		Active metabolite					0.5	392.42				−4.37	1.97	5	2	101.58
Sorafenib tosylate	200	mg	Tablets	Oral			0	464.83				−5.95	5.46	3	3	99.32
Spironolactone	100	mg	Tablets	Oral	0.022	18	0.5	416.58	−4.28	2.26	2.26	−4.58	2.65	3	0	63.61
Sulfamethoxazole	800	mg	Tablets	Oral	0.392	8.2	14	253.28	−2.81	0.89		−2.12	0.56	4	2	102.81

Table II. (Continued)

Generic name	Maximum strength dose value	Maximum strength dose unit	Formulation	Route	Measured solubility (mg/mL)	Dose number	% Excreted unchanged in urine	MW drug	Measured LogS molar	Measured LogP	Measured LogD74	minVSLgS 3–7.5	CLogP	HBA	HBD	PSA
Sulfasalazine	500	mg	Tablets	Oral	0.0024	833	1.5	398.40	−5.22		−0.78	−3.46	3.88	8	3	148.16
Sulfinpyrazone	200	mg	Capsules	Oral	0.031	26	39	404.49	−4.12	2.30	−0.08	−3.61	1.66	3	0	59.94
Sulindac	200	mg	Tablets	Oral	0.0028	286	1	356.42	−5.10	3.42	−0.66	−4.16	3.16	3	1	59.21
Sulindac sulfide		Active metabolite			0.0028		0.5	340.42	−5.08			−4.38	3.16	3	1	40.83
Tacrolimus	5	mg	Capsules	Oral	0.008	2.5	0.5	804.04	−5.00		3.96	−7.74	5.78	11	3	185.90
Tadalafil	20	mg	Tablets	Oral				389.41				−4.46	2.58	4	1	71.07
Tegaserod maleate	6	mg	Tablets	Oral			0.5	301.39				−3.06	2.81	5	4	88.12
Telithromycin	400	mg	Tablets	Oral	0.8	2.0	13	812.03	−3.01			−3.70	3.75	11	1	163.02
Telmisartan	80	mg	Tablets	Oral			0.5	514.63				−4.72	7.54	4	1	62.46
Temozolomide	250	mg	Capsules	Oral			5.6	194.15				−1.48	−0.81	5	1	101.89
Teniposide	10	mg/mL	Solution	Injection (i.v.)	0.025		9	656.67	−4.42	1.24	3.09	−5.24	0.72	12	3	166.64
Terbinafine	250	mg	Tablets	Oral				291.44		6.00		−4.71	5.96	1	0	1.18
Terfenadine	60	mg	Tablets	Oral	0.006	40	0	471.69	−4.90	5.69	4.77	−5.48	6.07	3	2	46.29
Testolactone	50	mg	Tablets	Oral	0.027	7.4		300.40	−4.05			−3.86	2.63	2	0	45.34
Testosterone	40	mg	Capsules	Oral	0.0234	6.8		288.43	−4.09	3.32		−3.92	3.22	2	1	40.83
Tetrabenazine	25	mg	Tablets	Oral			0	317.43				−2.41	3.81	4	0	37.66
Thalidomide	200	mg	Capsules	Oral	0.0525	15	0.5	258.24	−3.69	0.33		−2.54	0.53	4	1	88.83
Thiabendazole	500	mg	Tablets	Oral	0.05	40	0.1	201.25	−3.60	2.47		−3.01	2.36	2	1	34.46
Thyroxine; levothyroxine	0.3	mg	Tablets	Oral	0.000585	2.1	0	776.88	−6.12		0.65	−3.17	3.51	4	3	101.09
Tiagabine hydrochloride	16	mg	Tablets	Oral	0.03	2.1	2	375.56	−4.10			−1.87	2.78	3	1	42.01
Tiaprofenic acid	300	mg	Tablets	Oral			2.5	260.31		2.51	−0.86	−2.42	2.54	3	1	59.10
Tibolone	2.5	mg	Tablets	Oral			0	312.46				−4.68	3.15	2	1	40.83
Tipranavir	500	mg	Tablets	Oral			0.1	602.68				−6.52	7.76	5	2	111.66
Tizanidine	6	mg	Capsules	Oral				253.71				−2.40	2.09	5	2	58.53
Tolazamide	500	mg	Tablets	Oral	0.278	7.2		311.41	−3.05	2.69	0.09	−3.03	1.34	4	2	89.39
Tolbutamide	200	mg	Tablets	Oral	0.109	7.3	0	270.35	−3.39	2.34	2.52	−2.86	2.50	3	2	84.94
Tolcapone	200	mg	Tablets	Oral			0.5	273.25				−3.11	3.25	5	2	108.16
Tolfenamic acid	200	mg	Tablets	Oral			8	261.71		5.17		−3.55	5.66	3	2	54.80
Tolmetin	600	mg	Tablets	Oral	0.22	11	7	257.29	−3.07	2.79	−0.98	−2.29	2.21	3	1	59.67
Tolvaptan	30	mg	Tablets	Oral	0.0005	240	0	448.95	−5.95			−6.28	4.65	3	2	74.25
Torsemide, torasemide	100	mg	Tablets	Oral	0.16	1.56	20	348.43		3.37	0.45	−1.04	3.36	5	3	109.16
Trandolapril	4	mg	Tablets	Oral				430.55			1.08	−1.68	2.10	5	2	101.91
Trazodone	300	mg	Tablets	Oral	0.2	6.0	0.5	371.87	−3.27	3.80	2.64	−4.92	3.85	4	0	34.31
Treprostinil	10	mg/mL	Solution	Injection (s.c.)			4	390.52				−4.33	3.72	5	3	95.05
Tretinoin	10	mg	Capsules	Oral			0.5	300.44		6.30	4.23	−4.71	6.74	2	1	40.83
Triamterene	100	mg	Capsules	Oral	0.029	14	10	253.27	−3.94	0.98	1.30	−2.54	1.61	7	3	123.98
Triclabendazole	250	mg	Tablets	Oral	0.0002	5000	2	359.66	−6.25	2.31		−5.39	6.44	1	1	33.63
Trimipramine maleate	100	mg	Tablets	Oral				294.44			1.98	−2.35	5.44	2	0	1.75
Ursodiol; ursodeoxycholic acid	500	mg	Tablets	Oral			0.5	392.58		4.15	2.03	−4.68	4.51	4	3	85.95
Valdecoxib; bextra	20	mg	Tablets	Oral				314.37				−3.93	1.83	3	1	88.84
Vitamin A (retinol)	110	mg	Tablets	Oral	0.044	10	0	286.46	−3.81	5.68		−5.12	6.40	1	1	22.56
Vitamin D2 (ergocalciferol)	1.25	mg	Capsules	Oral				396.66		7.04		−6.63	9.39	1	1	22.56
Voriconazole	200	mg	Tablets	Oral	0.39	2.1	1.5	349.32	−2.95			−3.20	0.52	5	1	67.01
Warfarin	10	mg	Tablets	Oral	0.018	2.2	1	308.34	−4.23	2.60	1.12	−3.40	2.90	3	1	68.83
Zafirlukast	20	mg	Tablets	Oral			0	575.69				−6.67	7.09	6	2	121.38
Zaleplon	10	mg	Capsules	Oral			0.5	305.34		1.23		−4.19	1.44	5	0	61.50
Zileuton	600	mg	Tablets	Oral	0.5	4.8		236.29	−2.67			−2.16	2.48	2	2	73.18
Ziprasidone hydrochloride	80	mg	Capsules	Oral	0.00043	744	0.5	412.94	−5.98			−4.92	4.21	4	1	44.63

Table III. Measured and *In Silico* Data for 247 BDDCS Class 3 Drugs

Generic name	Maximum strength dose value	Maximum strength dose unit	Formulation	Route	Measured solubility (mg/mL)	Dose number	% Excreted unchanged in urine	MW drug	Measured LogS molar	Measured LogP	Measured LogD74	minVSLgS 3–7.5	CLogP	HBA	HBD	PSA
Acamprosaic acid	333	mg	Tablets	Oral			50	181.21				0.72	−2.47	4	2	92.63
Acecainide; *N*-acetyl procainamide		Active metabolite			50		81	277.37	−0.74			−0.91	1.64	3	2	66.56
Acrivastine	8	mg	Capsules	Oral	0.7	0.05	67	348.45	−2.70			−2.11	1.46	4	1	52.25
Adefovir dipivoxil	10	mg	Tablets	Oral	0.4	0.1	45	333.24	−2.92			−1.63	−1.98	8	3	149.47
Albuterol; salbutamol	4	mg	Tablets	Oral			50	239.32			−1.11	0.45	0.06	4	4	82.56
Alendronate sodium	70	mg	Tablets	Oral			45	249.10				4.87	−5.64	8	6	178.77
Almotriptan	12.5	mg	Tablets	Oral			40	335.47				−1.46	1.79	3	1	53.85
Alvimopan	12	mg	Capsules	Oral	0.1	0.5	2	424.54	−3.63			−1.82	2.16	5	3	97.72
Amantadine	100	mg	Capsules	Oral	50	0.008	85	151.25	−0.48	2.44	−0.69	2.00	2.00	1	1	27.97
Amikacin	250	mg/mL	Solution	Injection (i.v.)			98	585.61				5.31	−6.30	17	13	360.37
Amiloride	5	mg	Tablets	Oral	50	0.0004	49	229.63	−0.66	0.10	−1.25	−1.03	0.11	7	5	159.65
Aminocaproic acid	1000	mg	Tablets	Oral	333	0.01	65	131.18	0.40	−2.95	−1.60	2.05	−2.24	3	2	68.80
Amoxicillin	875	mg	Tablets	Oral	3.5	1.0	86	365.41	−2.02	0.87	−1.52	−0.47	−1.87	6	4	143.96
Ampicillin	500	mg	Capsules	Oral	7.8	0.3	88	349.41	−1.65	1.35	−1.61	−0.42	−1.20	5	3	121.09
Atenolol	100	mg	Tablets	Oral	24.8	0.02	94	266.34	−1.03	0.16	−1.03	−0.16	−0.11	4	3	92.48
Atropine (DL)	0.4	mg	Tablets	Oral	0.002	0.8	57	289.38	−5.16	1.83		−0.96	1.30	3	1	50.80
Azacitidine	25	mg/mL	Solution	Injection (i.v.)	89		62	244.21	−0.44	−3.02		−0.83	−2.20	8	4	143.47
Azithromycin	600	mg	Tablets	Oral	39	0.06	6	749.00	−1.28	4.02		−3.15	2.64	13	5	186.17
Azlocillin	4000	mg	Powder	Injection (i.v.)	50	0.3	65	461.50	−0.97			−2.82	1.56	6	4	159.99
Aztreonam	40	mg/mL	Solution	Injection (i.v.)	10		68	435.44	−1.64		−5.07	1.07	0.34	11	4	213.20
Baclofen	20	mg	Tablets	Oral	2.1	0.04	69	213.67	−2.01	−0.96	−0.96	0.91	−0.62	3	2	68.80
Benazeprilat		Active metabolite					18	396.45			−0.07	−0.89	2.04	6	3	115.38
Bendroflumethiazide	10	mg	Tablets	Oral	0.108	0.4	21	421.42	−3.59	1.89	1.99	−3.42	1.73	5	3	131.87
Betamipron	5	mg/mL	Solution (with panipenem)	Injection (i.v.)			98	193.20				−1.18	0.72	3	2	73.68
Biapenem	300	mg	Powder	Injection (i.v.)			53	350.40				−0.67	−6.35	5	1	97.13
Biotin	5	mg	Tablets	Oral	0.22	0.09	43	244.31	−3.05			−1.14	−0.08	3	3	88.25
Bisoprolol fumarate	10	mg	Tablets	Oral			63	325.45		1.87	−0.23	−1.52	1.83	5	2	63.82
Bleomycin A2	3	mg/mL	Solution	Injection (i.v.)	20		68	1415.58	−1.85			−7.03	−7.68	28	20	662.79
Bretylium	50	mg/mL	Solution	Injection (i.v.)	50		77	243.17	−0.69		−2.10	−1.93	−1.25	0	0	0.00
Bumetanide	2	mg	Tablets	Oral	0.1	0.08	45	364.42	−3.56		−0.45	−3.55	3.37	5	3	130.02
Cadralazine	10	mg	Tablets	Oral	1.3	0.03	75	283.33	−2.34		0.32	−2.80	0.93	6	3	106.01
Capreomycin 1B	500	mg/mL	Solution	Injection (i.v.)			90	653.70				1.99	−5.51	11	13	389.22
Captopril	100	mg	Tablets	Oral	160	0.003	38	217.29	−0.13	0.34	−1.98	−1.04	0.89	3	2	60.28
Carbenicillin	382	mg	Tablets	Oral	50	0.03	82	378.41	−0.88	1.13		−1.33	1.64	6	3	133.95
Carboplatin	10	mg/mL	Solution	Injection (i.v.)	14		77	371.26	−1.42	−2.30		0.94	−0.34	2	2	149.65
Carteolol	10	mg	Tablets	Oral			60	292.38			−0.46	−0.76	1.29	4	3	78.78
Cefaclor	500	mg	Capsules	Oral	8.59	0.2	52	367.81	−1.63		−1.76	−0.17	−1.64	5	3	121.09
Cefadroxil	1000	mg	Tablets	Oral	14.2	0.3	93	363.39	−1.41		−3.40	0.14	−2.51	6	4	143.96
Cefamandole	400	mg	Tablets	Oral	333	0.005	96	462.51	−0.14	0.50	−2.40	−2.54	0.11	8	3	155.70
Cefazolin	1000	mg	Powder	Injection (i.v.)	33	0.1	80	454.51	−1.14	−0.58	−3.14	−1.36	−1.19	9	2	156.53
Cefepime	2000	mg	Powder	Injection (i.v.)			85	480.57				−0.27	−3.05	8	2	152.65
Cefmetazole sodium	40	mg/mL	Solution	Injection (i.v.)	0.0942		80	471.54	−3.70	−0.60		−2.34	−1.34	9	2	160.63
Cefodizime	50	mg/mL	Solution	Injection (i.v.)	270		80	584.67	−0.34			−1.00	1.10	11	4	203.72
Cefonicid	20	mg/mL	Solution	Injection (i.v.)			99	542.57				−1.71	−1.92	11	4	215.48
Ceforanide	50	mg/mL	Solution	Injection (i.v.)			84	519.56				0.00	−3.36	10	4	201.94
Cefotaxime	40	mg/mL	Solution	Injection (i.v.)			30	455.47			−1.70	−0.31	0.14	9	3	179.71
Cefotetan	50	mg/mL	Solution	Injection (i.v.)			67	575.62			−1.20	−2.04	−1.54	11	4	229.00
Cefotiam	167	mg/mL	Solution	Injection (i.v.)			80	525.63				−0.79	−3.58	10	3	172.22
Cefoxitin	50	mg/mL	Solution	Injection (i.v.)	1000		85	427.46	0.37	−0.02	−1.89	−1.42	−0.81	6	3	156.95
Cefsulodin	500	mg	Powder	Injection (i.v.)	50	0.04	60	532.55	−1.03			−1.96	−6.89	8	3	199.72
Ceftazidime	20	mg/mL	Solution	Injection (i.v.)	5		85	546.58	−2.04	−1.60	−3.80	−0.46	−3.75	10	3	194.05
Ceftizoxime	40	mg/mL	Solution	Injection (i.v.)			93	383.41				0.41	0.34	8	3	152.65

Table III. (Continued)

Generic name	Maximum strength dose value	Maximum strength dose unit	Formulation	Route	Measured solubility (mg/mL)	Dose number	% Excreted unchanged in urine	MW drug	Measured LogS molar	Measured LogP	Measured LogD74	minVSLgS 3–7.5	CLogP	HBA	HBD	PSA
Ceftriaxone	40	mg/mL	Solution	Injection (i.v.)	400		46	554.59	−0.14		−4.30	0.31	0.02	12	4	216.88
Cefuroxime	50	mg	Tablets	Oral	200	0.001	96	424.39	−0.33	−0.16	−1.91	−1.76	0.23	7	3	179.19
Celiprolol	200	mg	Tablets	Oral	151	0.005	20	379.50	−0.40	1.92	1.14	−1.73	1.86	5	3	98.23
Cephalexin	750	mg	Capsules	Oral	12	0.3	91	347.40	−1.46	−0.67	−2.40	−0.28	−1.84	5	3	121.09
Cephalothin sodium	2000	mg	Powder	Injection (i.v.)	50	0.2	52	396.44	−0.92	0.00	−2.20	−1.72	−0.28	5	3	120.19
Cephapirin	1000	mg	Powder	Injection (i.v.)			48	423.47		−1.15	−1.15	−0.27	−0.61	6	2	130.43
Cephradine	500	mg	Capsules	Oral	26	0.08	86	349.41	−1.13	−1.75	−2.10	−0.07	−1.73	5	3	121.09
Cetirizine	10	mg	Tablets	Oral	0.101	0.4	50	388.90	−3.59	1.70	−0.31	−1.42	2.08	5	1	51.97
Chloroquine	500	mg	Tablets	Oral	100	0.02	61	319.88	−0.50	4.63	1.54	−1.17	5.06	3	1	25.69
Cidofovir	75	mg/mL	Solution	Injection (i.v.)	170		90	279.19	−0.22			2.99	−2.39	8	4	152.23
Cilastatin	250	mg/mL	Solution (with imipenem)	Injection (i.v.)	25		70	358.46	−1.16		−1.10	0.77	0.47	6	4	142.48
Cilazaprilat	2.6	mg	Tablets	Oral			91	389.46				1.01	1.50	7	3	120.13
Cimetidine	800	mg	Tablets	Oral	6.2	0.5	62	252.34	−1.61	0.40	0.33	−1.91	0.19	5	3	81.67
Clarithromycin	500	mg	Tablets	Oral	2	1.0	35	747.97	−2.57	3.16		−4.00	2.37	13	4	189.50
Clavulanic acid	125	mg	Tablets (with 875 mg amoxicillin)	Oral			43	199.16				0.31	−1.07	5	2	91.63
Clofarabine	1	mg/mL	Solution	Injection (i.v.)	1		55	303.68	−2.48			−1.97	−0.46	7	3	112.88
Clonidine	0.3	mg	Tablets	Oral			62	230.10		1.43	0.83	−1.46	1.73	3	2	38.46
Cromolyn	5.2	mg/inhalation	Solution	Topical (nasal)	210	0.0001	50	468.38	−0.35	1.92	−4.80	−2.33	1.48	11	3	177.81
Cycloserine	250	mg	Capsules	Oral	100	0.01	65	102.09	−0.01			1.25	−1.19	3	2	72.82
Dabigatran		Active metabolite					85	471.52				−2.28	0.06	8	4	146.28
Dacarbazine	10	mg/mL	Solution	Injection (i.v.)	4.2		39	182.19	−1.64	−0.24	−0.24	−1.56	0.48	5	2	97.62
Dactinomycin; actinomycin D	0.5	mg/mL	Solution	Injection (i.v.)	0.5		10	1255.45	−3.40			−6.89	8.01	18	5	368.53
Dalfampridine	10	mg	Tablets	Oral			90.3	94.12		0.26		1.51	0.32	2	1	37.91
Daptomycin	50	mg/mL	Solution	Injection (i.v.)	1000		40.5	1620.71	−0.21			−7.54	−2.43	27	22	774.05
Demeclocycline	300	mg	Tablets	Oral	1.5	0.8	47	464.86	−2.49	−0.60		0.39	−0.59	9	6	197.07
Desmopressin	0.2	mg	Tablets	Oral			47	1069.24				−2.48	−3.14	15	14	476.51
Desvenlafaxine	100	mg	Tablets	Oral	572	0.0007	45	263.38	0.34		0.21	−1.28	2.68	3	2	34.13
Dexrazoxane	500	mg	Powder	Injection (i.v.)	11	0.2	42	268.27	−1.39		−1.60	−2.12	−1.33	6	2	104.58
Dibekacin; dideoxykanamycin B	50	mg/mL	Ampoules	Injection (i.m.)			81	451.52				1.70	−3.41	13	9	265.26
Dicloxacillin	500	mg	Capsules	Oral			60	470.33		2.91		−3.36	2.98	5	2	116.46
Didanosine	25	mg	Tablets	Oral	27.3	0.004	55	236.23	−0.94	−1.24	−1.24	−1.62	−1.65	6	2	84.65
Digitoxin	0.1	mg	Tablets	Oral	0.01	0.04	30	764.96	−4.88	2.83	2.83	−6.01	2.85	12	5	192.62
Digoxin	0.25	mg	Tablets	Oral	0.986	0.001	60	780.96	−2.90	1.26	1.26	−6.30	1.42	13	6	215.17
Disopyramide	150	mg	Capsules	Oral	1	0.6	55	339.48	−2.53	2.58	−0.43	−0.79	2.58	3	1	57.66
Dofetilide	0.5	mg	Capsules	Oral			64	441.57				−3.35	1.99	6	2	113.88
Dorzolamide hydrochloride	0.02	mg/mL	Solution	Ophthalmic	3.9		10	324.44	−1.92			1.31	−0.43	5	2	116.83
Doxycycline	40	mg	Tablets	Oral			41	444.45		−0.02	−0.06	0.52	−0.51	9	6	197.07
Edetate calcium disodium	200	mg/mL	Solution	Injection (i.v.)	91		95	292.25	−0.51			6.61	−1.93	10	4	165.67
Emtricitabine	200	mg	Capsules	Oral	112	0.007	73	247.25	−0.34	−0.43	−0.43	−1.31	−1.29	5	2	88.11
Enalaprilat	8	mg	Tablets	Oral			60	348.40		−0.74	−0.28	0.21	0.88	6	3	115.68
Entecavir	1	mg	Tablets	Oral	2.4	0.002	70	277.29	−2.06			−2.13	−2.58	6	4	126.09
Eptifibatide	2	mg/mL	Solution	Injection (i.v.)	65		50	831.98	−1.11			−5.02	−2.86	12	11	350.27
Ertapenem sodium	1000	mg	Powder	Injection (i.v.)			38	475.52				−0.26	−1.82	8	5	170.78
Erythromycin (base)	500	mg	Tablets	Oral	2.1	1.0	5	733.95	−2.54	3.06		−3.84	1.61	13	5	203.27
Erythromycin lactobionate	50	mg/mL	Solution	Injection (i.v.)	20		5	1074.21	−1.73			−3.84	1.61	13	5	203.27
Ethambutol	400	mg	Tablets	Oral			79	204.31			−2.79	1.55	0.12	4	4	74.26
Etidronic acid	400	mg	Tablets	Oral			50	206.03			−8.86	4.72	−2.54	7	5	150.80
Etoposide	50	mg	Capsules	Oral	0.22	0.9	38	588.57	−3.43	0.60	0.60	−4.31	0.03	12	3	166.64
EXP-3174		Active metabolite					55	436.90				−1.50	5.59	6	2	105.06
Famotidine	40	mg	Tablets	Oral			67	337.45		−0.64	−1.50	−1.64	−1.17	8	6	179.34
Ferrous sulfate	182	mg	Capsules	Oral	570	0.001		151.91	0.57			3.65	−4.15	4	0	75.52

Fexofenadine; terfenadine carboxylate	180	mg	Tablets	Oral			25	501.67			2.68	−3.08	1.96	5	3	87.12
Flecainide	150	mg	Tablets	Oral	48.4	0.01	43	414.35	−0.93	3.78	1.14	−2.20	3.66	4	2	65.63
Fluconazole	200	mg	Capsules	Oral	1	0.8	75	306.28	−2.49	0.50	0.95	−2.35	−0.44	5	1	70.48
Flucytosine	500	mg	Capsules	Oral	15	0.1	99	129.09	−0.93		−1.97	0.05	−1.64	3	2	70.15
Foscarnet	24	mg/mL	Solution	Injection (i.v.)			82	126.01			−2.00	3.43	−2.17	5	3	104.95
Fosfomycin tromethamine	3000	mg	Tablets	Oral	50	0.2	82	138.06	−0.44			4.57	−0.23	4	2	72.91
Gabapentin	800	mg	Tablets	Oral	10	0.3	100	171.24	−1.23	−1.10	−1.31	1.75	−0.66	3	2	68.80
Gallium nitrate	25	mg/mL	Solution	Injection (i.v.)			80	255.73				1.71	1.43	9	0	199.71
Ganciclovir sodium	500	mg	Capsules	Oral	6	0.3	91	255.24	−1.66	−1.66	−4.25	−1.52	−2.73	8	4	134.88
Gentamicin C1 sulfate	40	mg/mL	Solution	Injection (i.v.)	50		91	477.61	−0.98		−8.40	3.49	−1.80	12	8	215.91
Gold sodium thiomalate	50	mg/mL	Solution	Injection (i.m.)			70	368.09				1.90	−3.30	4	1	81.66
Guanfacine hydrochloride	2	mg	Tablets	Oral	1	0.008	50	246.10	−2.39	1.33	1.12	−2.16	1.37	3	3	83.82
Hydrochlorothiazide	50	mg	Tablets	Oral	0.6	0.3	100	297.74	−2.70	−0.07	−0.07	−1.75	−0.37	5	3	131.87
Hydrodolasetron		Active metabolite					53	326.40				−1.44	1.90	3	2	64.77
Hydroflumethiazide	50	mg	Tablets	Oral	0.3	0.7	90	331.29	−3.04	0.36	0.36	−1.88	−0.21	5	3	131.87
Hydroxyurea	1000	mg	Tablets	Oral	50	0.08	80	76.06	−0.18	−1.80		1.19	−1.80	2	3	86.58
Hyoscyamine; L-atropine	311	μg	Tablets	Oral	3.56	0.0003	57	289.38	−1.91	1.83	−0.44	−0.88	1.30	3	1	50.80
Ibandronate	150	mg	Tablets	Oral			55	319.23				2.10	−3.37	8	5	151.98
Imidaprilat		Active metabolite					9	377.40				0.46	1.74	7	3	137.49
Imipenem	750	mg	Powder	Injection (i.v.)	10	0.3	69	299.35	−1.48			0.82	−1.35	6	4	120.42
Iohexol	755	mg/mL	Solution (equivalent to 350 mg I per mL)	Injection (i.v.)			95	821.15				−4.12	0.66	9	8	220.19
Iopamidol	755	mg/mL	Solution (equivalent to 370 mg I per mL)	Injection (i.v.)			96	777.09				−3.88	0.86	8	8	211.03
Iopromide	769	mg/mL	Solution (equivalent to 370 mg I per mL)	Injection (i.v.)			97	791.12				−3.90	1.37	8	6	183.86
Ipratropium bromide	17	μg/activation	Solution	Topical (aerosol)			50	332.47				−2.28	−2.19	2	1	49.62
Kanamycin	333	mg/mL	Solution	Injection (i.v.)			90	484.51				3.84	−5.17	15	11	304.97
Ketorolac	10	mg	Tablets	Oral	200	0.0002	58	255.28	−0.11	1.04		−2.37	1.62	3	1	59.67
Lacosamide; erlosamide	50	mg	Tablets	Oral	2	0.1	40	250.30	−2.10			−2.15	0.39	3	2	74.48
Lamivudine	300	mg	Tablets	Oral	70	0.02	67	229.26	−0.52	−0.93		−1.21	−1.46	5	2	88.11
Latamoxef; moxalactam	100	mg/mL	Solution	Injection (i.v.)	50		76	520.48	−1.02	−0.58	−3.45	−1.98	−0.82	12	4	214.42
Leucovorin; folinic acid	25	mg	Tablets	Oral	500	0.0002	10	473.45	0.02		−7.85	−1.81	−3.49	12	7	232.35
Levalbuterol	45	μg/activation	Solution	Topical (aerosol)	180	0.000001	46	239.32	−0.12		−1.11	0.45	0.06	4	4	82.56
Levetiracetam	1000	mg	Tablets	Oral	1040	0.004	66	170.21	0.79			−1.18	−0.34	2	1	65.69
Levocetirizine	5	mg	Tablets	Oral	0.101	0.2	71	388.90	−3.59	1.70	−0.31	−1.54	2.08	5	1	51.97
Levofloxacin	750	mg	Tablets	Oral	50	0.06	74	361.38	−0.86	−0.39	−0.40	−0.45	−0.51	7	1	70.83
Lincomycin	300	mg/mL	Solution	Injection (i.v.)	50		30	406.55	−0.91	0.56		−2.27	1.28	7	5	133.05
Lisinopril	40	mg	Tablets	Oral	97	0.002	94	405.50	−0.62	−1.22	−3.40	1.85	−1.69	7	4	143.65
Lithium carbonate	600	mg	Tablets	Oral	13	0.2	95	73.89	−0.75			0.00	−3.65	3	0	63.19
Lomefloxacin	400	mg	Tablets	Oral	1.64	1.0	65	351.36	−2.33	−0.30	−1.03	−0.56	−0.11	6	2	75.12
Loperamide	2	mg	Capsules	Oral	1.4	0.006	0.5	477.05	−2.53		4.22	−4.57	4.66	3	1	43.18
Loracarbef	400	mg	Capsules	Oral	41	0.04	94	349.78	−0.93			−0.36	−0.47	5	3	121.09
Memantine	10	mg	Tablets	Oral			71	179.31		3.28		1.35	3.03	1	1	27.97
Metformin	1000	mg	Tablets	Oral			99	129.17			−5.41	4.13	−1.63	5	4	89.74
Methazolamide	50	mg	Tablets	Oral	0.704	0.3	61	236.27	−2.53	0.13		−1.04	0.09	6	1	107.10
Methicillin	40	mg/mL	Solution	Injection (i.v.)	300		88	380.42	−0.10	1.22	−2.41	−2.39	1.78	6	2	111.33
Methotrexate	15	mg	Tablets	Oral	0.45	0.1	81	454.45	−3.00	−1.85	−2.52	−0.03	−0.53	12	5	211.69
Methyldopa	500	mg	Tablets	Oral	10	0.2	40	211.22	−1.32	0.39	−2.39	1.34	−2.26	5	4	114.54
Methylnaltrexone	20	mg/mL	Solution	Injection (s.c.)			52.75	356.45		−1.12	−1.12	−1.70	−2.64	4	2	72.81
Metoclopramide	10	mg	Tablets	Oral	0.2	0.2	20	299.80	−3.18	2.62	0.32	−1.25	2.23	4	2	70.79
Metocurine iodide	2	mg/mL	Solution	Injection (i.v.)	3		50	652.84	−2.34			−5.31	1.12	4	0	55.25
Mezlocillin	2000	mg	Powder	Injection (i.v.)			45	539.59				−3.36	1.50	8	3	184.12
Miglitol	100	mg	Tablets	Oral			80	207.23		−3.21		1.70	−1.26	6	5	113.97
Miglustat	100	mg	Capsules	Oral	1000	0.0004	85	219.28	0.66			0.22	0.91	5	4	91.41
Milnacipran	100	mg	Tablets	Oral			55	246.36				1.46	1.91	2	1	47.42
Milrinone	1	mg/mL	Solution	Injection (i.v.)	1		85	211.23	−2.32		0.68	−2.50	−0.03	3	1	61.18

Table III. (Continued)

Generic name	Maximum strength dose value	Maximum strength dose unit	Formulation	Route	Measured solubility (mg/mL)	Dose number	% Excreted unchanged in urine	MW drug	Measured LogS molar	Measured LogP	Measured LogD74	minVSLgS 3–7.5	CLogP	HBA	HBD	PSA
Mitoxantrone	2	mg/mL	Solution	Injection (i.v.)	7.5		7	444.49	−1.77		0.70	−0.60	2.30	10	8	185.09
Morphine 6-glucuronide		Active metabolite			1000		90	461.47	0.34		−0.66	−0.23	−3.10	10	5	159.24
Moxifloxacin hydrochloride	400	mg	Tablets	Oral	27.5	0.06	22	401.44	−1.20			−0.83	−0.08	7	2	84.22
Nadolol	160	mg	Tablets	Oral	30.4	0.02	73	309.41	−1.01	0.81	0.93	−0.39	0.38	5	4	91.35
Nafcillin sodium	36	mg/mL	Solution	Injection (i.v.)			27	414.48				−3.46	3.53	5	2	102.23
Naratriptan	2.5	mg	Tablets	Oral	35	0.0003	50	335.47	−0.98			−0.72	1.70	3	2	67.24
Neomycin B sulfate	500	mg	Tablets	Oral	6.3	0.3	40	614.66	−2.05			4.21	−6.47	19	13	378.50
Neostigmine	15	mg	Tablets	Oral	100	0.0006	67	223.30	−0.35			−0.51	−2.81	1	0	28.55
Netilmicin	100	mg/mL	Solution	Injection (i.v.)			85	475.59				2.52	−2.40	12	8	215.91
Nizatidine	300	mg	Capsules	Oral	21.65	0.06	61	331.46	−1.18	−0.20	1.00	−2.55	−0.16	6	2	85.02
Nystatin	200	mg	Capsules	Oral	4	0.2		926.12	−2.36			−6.39	−3.20	17	12	347.83
Ofloxacin	400	mg	Tablets	Oral	3.54	0.5	64	361.38	−2.01	−0.39	−0.40	−0.57	−0.51	7	1	70.83
Olmesartan		Active metabolite					43	446.51				−2.31	2.51	7	3	127.62
Olopatadine hydrochloride	5	mg	Tablets	Ophthalmic	2	0.01	65	337.42	−2.23			−1.06	1.09	4	1	51.11
Oseltamivir		Active metabolite					99	284.36				0.57	−1.24	5	3	110.44
Oxacillin	167	mg/mL	Solution	Injection (i.v.)			46	401.44		2.38	−1.24	−2.86	2.05	5	2	116.46
Palonosetron hydrochloride	0.05	mg/mL	Solution	Injection (i.v.)			40	296.42				−2.72	2.18	2	0	20.62
Pamidronate disodium	15	mg/mL	Solution	Injection (i.v.)			46	235.07			−7.87	5.20	−6.17	8	6	178.77
Pancuronium bromide	2	mg/mL	Solution	Injection (i.v.)			67	572.88				−4.27	1.21	2	0	54.13
Pemetrexed disodium	25	mg/mL	Solution	Injection (i.v.)	90		80	427.42	−0.68			−2.23	−1.17	9	6	198.63
Penciclovir	10	mg/g	Cream	Topical (skin, membranes)	170		75	253.26	−0.17	−1.62		−2.17	−2.72	6	4	126.09
Penicillamine	250	mg	Capsules	Oral			45	149.21		−1.78	−3.94	2.60	−1.73	3	3	68.80
Penicillin G; benzylpenicillin	39 (60,000	mg/mL units/mL)	Solution (as potassium salt)	Injection (i.v.)				334.40		1.83	−1.81	−2.21	1.75	4	2	93.12
Pentostatin	2	mg/mL	Solution	Injection (i.v.)	30		80	268.27	−0.95	−2.09	−4.65	−1.17	−1.96	7	4	111.17
Phenylethylmalonamide	250	mg	Tablets	Oral			79	206.25		0.13	0.13	−1.61	0.01	2	2	92.49
Phenylpropanolamine	75	mg	Tablets	Oral			65	151.21		0.83	−2.27	0.99	0.58	2	2	50.53
Pindolol	10	mg	Tablets	Oral	7.9	0.005	54	248.33	−1.50	1.75	0.39	−1.40	1.67	3	3	60.21
Pipecuronium bromide	1	mg/mL	Solution	Injection (i.v.)			39	602.91				−3.57	0.63	4	0	56.48
Piperacillin	200	mg/mL	Solution (with 25 mg/mL tazobactam)	Injection (i.v.)	714.3		71	517.56	0.14	0.50	−3.30	−3.44	1.70	7	3	164.86
Piperazine	500	mg	Tablets	Oral	260	0.008	50	86.14	0.48	−1.50		3.10	−1.48	2	2	29.15
Piracetam	800	mg	Tablets	Oral			70	142.16		−1.54	−1.55	−0.45	−1.18	2	1	65.69
Pirenzepine	50	mg	Tablets	Oral	50	0.004	43	351.41	−0.85	0.10	−0.39	−3.12	−0.35	5	1	63.98
Plerixafor	20	mg/mL	Solution	Injection (s.c.)	10		70	502.80	−1.70			4.68	−0.25	8	6	89.79
Potassium chloride	1500	mg	Tablets	Oral	333.3	0.02	85	74.56	0.65			−1.07	−2.14	0	0	0.00
Pramipexole	1.5	mg	Tablets	Oral	0.2	0.03	90	211.33	−3.02			0.66	1.17	3	2	52.49
Pravastatin	80	mg	Tablets	Oral	300	0.001	20	424.54	−0.15	2.18	−0.23	−3.75	2.05	6	4	135.57
Pregabalin	300	mg	Tablets	Oral	33	0.04	90	159.23	−0.68		−1.35	2.11	−0.92	3	2	68.80
Procainamide	1000	mg	Tablets	Oral	4	1.0	67	235.33	−1.77	0.88	−1.15	−0.52	1.42	3	2	61.69
Pseudoephedrine	120	mg	Tablets (discontinued; 60 mg in combinations)	Oral			43	165.24		1.13		0.80	0.89	2	2	37.13
Pyridostigmine	60	mg	Tablets	Oral	100	0.002	85	181.22	−0.26			−0.13	−4.26	1	0	29.12
Pyrimethamine	25	mg	Tablets	Oral	0.121	0.8	65	248.72	−3.31	2.69	1.61	−2.91	3.00	4	2	75.82
Quinaprilat		Active metabolite					96	410.47				−0.50	1.95	6	3	115.68
Raltitrexed	0.5	mg/mL	Solution	Injection (i.v.)			50	458.50				−0.32	0.71	8	4	157.86
Ramiprilat		Active metabolite					13	388.47				−0.28	1.75	6	3	115.68
Ranitidine	300	mg	Tablets	Oral	555	0.002	30	314.41	0.25	0.27	0.54	−1.50	0.67	5	2	84.19
Regadenoson	0.08	mg/mL	Solution	Injection (i.v.)	0.05		65	390.36	−3.89			−3.00	−2.86	10	5	181.70

Risedronate	150	mg	Tablets	Oral			87	283.12				2.80	−2.62	8	5	161.04
Ritodrine	10	mg	Tablets	Oral			10	287.36				−1.42	1.65	4	4	82.87
Rocuronium bromide	10	mg/mL	Solution	Injection (i.v.)			17	530.80				−3.53	6.40	0	0	59.59
Rolitetracycline	250	mg	Tablets	Oral	1250	0.0008	55	527.58	0.37		−3.21	−0.82	0.47	10	6	184.85
Rosuvastatin calcium	40	mg	Tablets	Oral			5	481.55			−0.89	−3.71	1.90	8	3	144.83
Roxatidine		Active metabolite					57.5	306.40				−2.62	2.35	4	1	65.68
Saxagliptin	5	mg	Tablets	Oral	17.6	0.001	24	315.42	−1.25			−2.48	0.11	4	2	88.67
Sitafloxacin	50	mg	Tablets	Oral			75	409.82				−1.33	−1.25	6	2	120.37
Sitagliptin	100	mg	Tablets	Oral			78	407.32				−1.70	0.69	4	1	71.38
Sotalol	240	mg	Tablets	Oral	137	0.007	85	272.37	−0.30	0.24	−0.79	0.11	0.23	4	3	88.93
Spectinomycin	625	mg/mL	Solution	Injection (i.m.)	7.5		70	332.36	−1.65			1.31	−2.88	9	5	141.47
Stavudine	40	mg	Capsules	Oral	83	0.002	39	224.22	−0.43	0.14		−1.60	−0.49	4	2	82.44
Streptomycin	1000	mg	Powder	Injection (i.m.)	20	0.2	55	581.58	−1.46			2.10	−4.26	19	14	357.04
Sulpiride	200	mg	Tablets	Oral	2.28	0.4	70	341.43	−2.18	0.57	−1.15	−0.99	1.11	5	2	108.62
Talinolol	100	mg	Tablets	Oral	1.23	0.3	52.8	363.50	−2.47			−2.27	3.15	4	4	93.35
Tazobactam sodium	25	mg/mL	Solution (with 200 mg/mL piperacillin)	Injection (i.v.)	50		77	300.29	−0.78			−0.42	−0.65	7	1	123.90
Temocaprilat		Active metabolite					29.5	448.56				−1.22	2.56	6	3	117.18
Temocillin disodium	100	mg/mL	Solution	Injection (i.v.)				414.46				−1.32	1.52	7	3	142.75
Tenofovir disoproxil	300	mg	Tablets	Oral	13.4	0.09	82	519.45	−1.59		1.25	−3.71	0.80	10	1	176.07
Terbutaline	5	mg	Tablets	Oral	213	0.00009	56	225.29	−0.02	0.90		1.54	0.48	4	4	82.87
Tetracycline	25	mg/mL	Syrup	Oral	1.7		58	444.45	−2.42	−1.30	−1.41		−0.91	9	6	197.07
Tetracycline hydrochloride	500	mg	Capsules	Oral	10.9	0.2	58	480.94	−1.64	−1.30	−1.41	0.66	−0.91	9	6	197.07
Ticarcillin	30	mg/mL	Solution	Injection (i.v.)	1000		77	384.43	0.42			−1.17	1.28	6	3	133.95
Tigecycline	10	mg/mL	Solution	Injection (i.v.)	295		22	569.66	−0.29			0.83	−0.83	10	5	195.34
Tiludronic acid	200	mg	Tablets	Oral			60	318.61				0.07	0.26	6	4	128.24
Tiotropium bromide	18	μg	Capsules	Oral			74	392.52				−1.64	−1.71	3	1	58.42
Tirofiban hydrochloride	0.05	mg/mL	Solution	Injection (i.v.)			65	440.61				−2.34	2.00	6	3	116.61
Tobramycin	40	mg/mL	Solution	Injection (i.v.)	1000		93	467.52	0.33			2.92	−4.72	14	10	287.82
Tocainide	600	mg	Tablets	Oral	10	0.2	38	192.26	−1.28	0.76	0.83	−0.94	0.26	2	2	60.51
Topiramate	200	mg	Tablets	Oral	9.8	0.08	70	339.37	−1.54			−2.05	0.04	8	1	118.72
Topotecan	1	mg	Capsules	Oral	1	0.004	40	421.46	−2.62			−0.91	0.73	6	2	102.76
Trimetazidine	20	mg	Tablets	Oral			62	266.34				0.04	1.18	5	1	43.06
Trimethoprim	160	mg	Tablets	Oral	1.37	0.5	70	290.32	−2.33	0.91	0.83	−2.25	0.98	7	2	103.14
Triptorelin	3.75	mg	Powder	Injection (i.m.)			41.7	1311.48				−5.29	−1.22	17	18	510.46
Trospium chloride	20	mg	Tablets	Oral	500	0.0002	6	392.52	0.11			−3.50	−1.16	2	1	49.62
Tubocurarine	3	mg/mL	Solution	Injection (i.v.)	50		63	609.75	−1.09			−2.82	3.55	5	2	83.96
Vancomycin	250	mg	Capsules	Oral	50	0.02	79	1449.29	−1.46			−7.43	−1.14	24	19	584.97
Varenicline tartrate	1	mg	Tablets	Oral	0.2	0.02	92	211.27	−3.02			−0.28	0.90	3	1	35.06
Vecuronium bromide	2	mg/mL	Solution	Injection (i.v.)			20	557.84				−3.70	4.33	3	0	55.30
Vigabatrin	500	mg	Tablets	Oral			60	129.16		−2.16	−2.60	2.68	−2.22	3	2	68.80
Vitamin B1 (thiamine)	500	mg	Tablets	Oral	27	0.07	90	265.36	−0.99			−1.58	−5.97	4	2	71.29
Zalcitabine	0.75	mg	Tablets	Oral	76.4	0.00004	65	211.22	−0.44	−1.30	−1.64	−1.24	−1.25	5	2	88.11
Zanamivir	5	mg	Powder	Topical (aerosol)	18	0.001	100	332.32	−1.27			1.76	−5.56	10	8	215.70
Zoledronic acid	0.8	mg/mL	Solution	Injection (i.v.)			39	272.09				3.16	−3.07	8	5	161.62

Table IV. Measured and *In Silico* Data for 53 BDDCS Class 4 Drugs

Generic name	Maximum strength dose value	Maximum strength dose unit	Formulation	Route	Measured solubility (mg/mL)	Dose number	% Excreted unchanged in urine	MW drug	Measured LogS molar	Measured LogP	Measured LogD74	minVSLgS 3–7.5	CLogP	HBA	HBD	PSA
Acetazolamide	250	mg	Tablets	Oral	0.64	1.6	90	222.25	−2.54	−0.26	−0.45	−0.77	−0.98	5	2	121.43
Acyclovir	800	mg	Tablets	Oral	2.5	1.3	75	225.21	−1.95	−1.56	−1.76	−2.68	−2.42	6	3	112.32
Amisulpride	200	mg	Tablets	Oral			50	369.49		1.10		−1.30	1.80	6	2	107.55
Atovaquone	250	mg	Tablets	Oral			3	366.85			3.82	−5.06	6.35	3	1	59.10
Auranofin	3	mg	Capsules	Oral			60	678.49				−1.91	3.79	5	0	117.05
Azapropazone; apazone	300	mg	Capsules	Oral	0.0615	20	60	300.36	−3.69	1.78		−3.35	1.79	4	0	52.35
Candesartan		Active metabolite					52	440.47				−2.11	5.43	7	2	114.16
Candesartan cilexetil	32	mg	Tablets	Oral	0.05	2.6	0	610.68	−4.09			−4.35	7.33	8	1	136.25
Cefdinir	300	mg	Capsules	Oral			15	395.42				0.27	−0.48	8	4	166.41
Cefditoren		Active metabolite					70	506.58				−6.73	1.46	9	2	162.89
Cefixime	400	mg	Capsules	Oral	0.05511	29	41	453.46	−3.92			0.91	0.25	10	4	193.48
Cefpodoxime	200	mg	Tablets	Oral			81	427.46				0.09	−0.41	9	3	155.91
Cefprozil	500	mg	Tablets	Oral	0.055	36	73	389.43	−3.85			−0.49	−1.87	6	4	143.96
Ceftibuten	400	mg	Capsules	Oral	0.08	20	71	410.43	−3.71			1.68	−1.21	8	4	171.87
Chlorothiazide	500	mg	Tablets	Oral	0.52	3.8	92	295.72	−2.75	−0.24	−1.10	−1.59	−1.00	6	2	126.91
Chlorthalidone	100	mg	Tablets	Oral	0.27	1.5	65	338.77	−3.10	0.85	0.85	−2.98	0.45	4	3	120.90
Cinoxacin	500	mg	Tablets	Oral			60	262.22			−1.55	−2.05	1.74	7	1	91.03
Ciprofloxacin	750	mg	Tablets	Oral	0.15	20	65	331.35	−3.34	0.28	−1.21	−0.45	−0.73	6	2	75.12
Clodronic acid	800	mg	Capsules	Oral	0.395	8.1	80	244.89	−2.79			4.95	−0.14	6	4	128.24
Cloxacillin	250	mg	Tablets	Oral	0.0139	72	75	435.89	−4.50	2.48	−1.82	−2.98	2.52	5	2	116.46
Dalfopristin	100	mg/mL	Solution	Injection (i.v.)			4.5	690.86				−5.35	0.92	9	2	177.78
Daunorubicinol		Active metabolite					25	529.55				−1.12	1.36	11	6	204.62
Enoxacin	400	mg	Tablets	Oral	0.6	2.7	45	320.33	−2.73	−0.20	−2.15	0.07	−1.60	7	2	85.36
Eprosartan	600	mg	Tablets	Oral	0.08	30	30	424.52	−3.72			−4.18	4.80	5	2	92.48
Erythromycin stearate	500	mg	Tablets	Oral	0.33	6.1	5	1018.40	−3.49			−3.84	1.61	13	5	203.27
Felbamate	600	mg	Tablets	Oral	0.7	3.4	45	238.25	−2.53		−0.29	−1.93	0.50	2	2	110.07
Fleroxacin	800	mg	Tablets	Oral	0.87	3.7	72.5	369.35	−2.63	0.24		−0.27	−0.33	6	1	61.72
Fosinoprilat		Active metabolite			0.01		43	435.50	−4.64		−0.69	−4.22	4.85	5	2	101.70
Furosemide	80	mg	Tablets	Oral			66	330.75		2.03	−1.54	−2.38	1.90	5	3	130.02
Iopanoic acid; iodopanoic acid	500	mg	Tablets	Oral	0.015	133	33	570.94	−4.58			−4.31	4.70	3	2	68.50
Lenalidomide	25	mg	Capsules	Oral	0.00045	222	66	259.27	−5.76			−2.64	0.53	4	2	88.83
Levocabastine	0.5	mg/mL	Solution	Ophthalmic			70	420.53				−2.60	1.86	4	1	60.70
Levonorgestrel	0.75	mg	Tablets	Oral	0.0014	2.1	52	312.46	−5.35		3.60	−4.34	3.31	2	1	40.83
Medroxyprogesterone acetate	500	mg	Tablets	Oral	0.022	91	44	386.54	−4.24			−4.69	4.01	3	0	63.61
Megestrol acetate	40	mg	Tablets	Oral	0.002	80	60	384.52	−5.28			−4.57	3.58	3	0	63.61
Meropenem	333.3	mg/mL	Solution	Injection (i.v.)			70	383.47				0.11	−3.28	6	3	116.86
Niclosamide	500	mg	Tablets	Oral	0.013	154		327.13	−4.40			−4.10	4.34	4	2	99.56
Nitrofurantoin	100	mg	Capsules	Oral	0.19	2.1	47	238.16	−3.10	−0.47	−0.19	−1.74	−0.47	5	1	118.74
Norfloxacin	400	mg	Tablets	Oral	0.75	2.1	29	319.34	−2.63	−1.03	−2.00	−0.32	−0.78	6	2	75.12
Orlistat	120	mg	Capsules	Oral			1	495.75				−7.63	8.61	3	1	86.97
Paliperidone	9	mg	Tablets	Oral	0.01125	3.2	59	426.50	−4.58		2.52	−2.77	1.12	5	1	76.16
Penicillin V; phenoxymethylpenicillin	500	mg	Capsules	Oral	0.25	8.0		350.40	−3.15	2.09	−1.54	−2.34	1.94	5	2	102.23
Phenazopyridine hydrochloride	200	mg	Tablets	Oral			41	213.24				−2.37	2.05	5	2	88.00
Quinupristin	100	mg/mL	Solution	Injection (i.v.)			3.5	1021.26				−6.15	7.05	12	4	236.20
Rifaximin	550	mg	Tablets	Oral	0.001	2200	0.035	785.90	−5.90			−7.16	7.24	12	5	205.94
Roxithromycin	300	mg	Tablets	Oral	0.1	12	12	837.07	−3.92	2.75		−4.95	2.29	16	5	224.19
Sulfadiazine	500	mg	Tablets	Oral	0.13	15	57	250.28	−3.28	−0.09	−1.00	−1.93	0.10	5	2	99.95
Sulfamethizole	500	mg	Tablets	Oral	0.25	8.0	86	270.33	−3.03	0.54	−1.11	−1.90	0.42	5	2	102.86
Sulfisoxazole	500	mg	Tablets	Oral	0.13	15	49	267.31	−3.31	1.01	−0.87	−2.01	0.22	4	2	102.81
Trandolaprilat		Active metabolite						402.49				−0.72	2.31	6	3	115.68
Triclabendazole sulfoxide		Active metabolite					6.5	375.66				−4.52	4.36	1	1	52.01
Valsartan	320	mg	Tablets	Oral	0.18	7.1	13	435.53	−3.38			−4.77	4.86	6	2	113.69
Vitamin B2 (riboflavin)	100	mg	Tablets	Oral	0.11	3.6	75	376.37	−3.53	−1.46		−2.64	−0.73	9	5	161.81

Table V. Measured and *In Silico* Data for 11 BDDCS Class 0 Drugs

Generic name	Maximum strength dose value	Maximum strength dose unit	Formulation	Route	Measured solubility (mg/mL)	Dose number	% Excreted unchanged in urine	MW drug	Measured LogS molar	Measured LogP	Measured LogD74	minVSLgS 3–7.5	CLogP	HBA	HBD	PSA
Amphetamine sulfate	10	mg	Tablets	Oral	30	0.001	40	135.21	−0.65	1.76	1.54	1.25	1.74	1	1	27.97
Atracurium	10	mg/mL	Solution	Injection (i.v.)			8.5	929.17				−7.00	3.50	10	0	126.97
Chlorphentermine	25	mg	Tablets	Oral			17	183.68		2.60	0.40	0.41	2.85	1	1	27.97
Chlorpropamide	250	mg	Tablets	Oral	2.2	0.5	20	276.74	−2.10	2.27	−0.13	−2.66	2.35	3	2	84.94
Cisatracurium besylate	10	mg/mL	Solution	Injection (i.v.)			8.5	929.17				−7.56	3.50	10	0	126.97
Dextroamphetamine	15	mg	Tablets	Oral	1	0.06	40	135.21	−2.13	1.76	1.54	1.29	1.74	1	1	27.97
Diethylcarbamazine citrate	100	mg	Tablets	Oral	63.7	0.006	35	199.30	−0.50		1.08	−0.69	1.62	2	0	21.80
Mecamylamine	2.5	mg	Tablets	Oral	212	0.00005	50	167.30	0.10			1.77	2.83	1	1	14.57
Methamphetamine	5	mg	Tablets	Oral	1000	0.00002	40	149.24	0.83			0.99	1.89	1	1	14.57
Phenmetrazine	25	mg	Tablets	Oral	2.5		19	177.25	−1.85	1.50		−0.20	1.67	2	1	23.37
Vitamin C, ascorbic acid	1000	mg	Capsules	Oral	333	0.01	25	176.13	0.28	−1.85		0.92	−1.76	5	4	117.30

the lowest solubility under the conditions listed above. The solubility criteria over the pH range 1–7.5 can create marked differences from compilation to compilation for drugs that are salts. For example, one may find in the package insert for atazanavir sulfate that the drug "is slightly soluble in water (4–5 mg/mL, free base equivalent) with the pH of a saturated solution in water being about 1.9." Reporting this solubility would lead to the assignment of atazanavir sulfate as a class 1 drug in BCS and BDDCS. However, it is known that atazanavir, as for almost all the protease inhibitors, exhibits very poor solubility in solutions at pH above 5.5, although these solubilities are not reported. Therefore, we list atazanavir sulfate as a class 2 drug and no specific solubility is listed in Table II. Another example of a basic drug is imatinib mesylate (and other kinase inhibitors) where the package insert states "Imatinib mesylate is soluble in aqueous buffers ≤pH 5.5 [a published value of 200 mg/mL can be found] but is very slightly soluble to insoluble in neutral/alkaline aqueous buffers." Therefore, we list this drug in Table II as class 2 with a solubility of 1 mg/mL, determined at pH 7.4. Similar variances can occur for acidic drugs where solubility may be very low at pH 1. This concern that the pH range maybe too restrictive has been addressed (34) and explicated (35) previously for acidic drugs. Individual references are not given for the solubility values because in many cases the values in the tables are the authors' consensus view of the appropriate value based on a number of experimental results as discussed above. This is a technique followed by Dr. Benet when he first introduced the table of pharmacokinetic parameters in Goodman and Gilman and represents a decision of the two senior authors alone in reviewing all of the literature data that they could find. A single solubility value is given in the five tables in milligrams per milliliter.

Figure 3 depicts a box plot of the measured solubility values (representing about 68% of drugs listed in Tables I, II, III, and IV) used for assigning BDDCS classification. Class 2 and 4 drugs are less soluble than class 1 and 3 drugs, but there

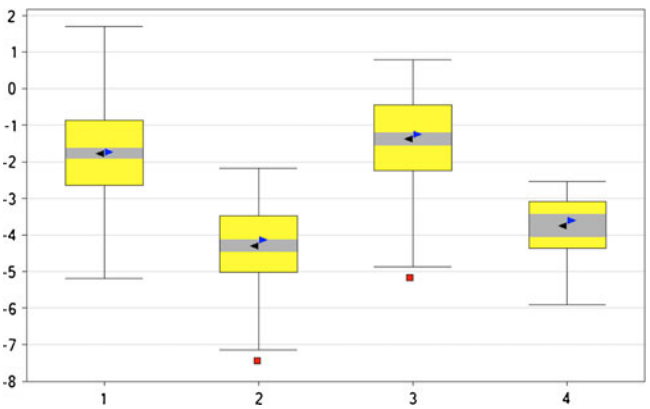

Fig. 3. Box plot of Log10 measured molar solubility values used for the BDDCS classification against BDDCS categories. *Arrows pointing left* show the mean, *arrows pointing right* the median; the *shaded area* indicates the 95% confidence interval, while the *box* itself is the interquartile range; the *horizontal bars* indicate the minimum and maximum values; *squares* are outliers. Class 1, −1.79±1.27 (266 drugs); class 2, −4.29±1.12 (167); class 3, −1.38±1.18 (159); class 4, −3.70±0.96 (35)

is a considerable overlap since the highest dose strength also affects the assignment. Further analysis with respect to the *in silico* predicted solubility values is addressed below.

Percent Excreted Unchanged in the Urine (%Urine)

Although the FDA (4) and EMA (9) guidances list 90% and 85% absorption, respectively, as a cutoff for high permeability, Wu and Benet (1) believed that a 70% cutoff for BDDCS would be sufficient since the purpose of BDDCS was not to provide a regulatory exemption but rather to make a prediction of drug disposition. As noted above, Wu and Benet (1) found that there were very few drugs in which the percent of dose metabolized fell between 30% and 70%. One may be tempted to use the percent urine values in the tables to test this hypothesis, but this would be incorrect since a number of class 3 and class 4 drugs are known to be excreted unchanged in the bile, as are the metabolites of some class 2 and possibly class 1 drugs, depending on the BDDCS class of the metabolite. When a drug is given intravenously, the percent of drug unchanged in the urine is readily obtained. When for a given drug only the oral dosage forms are available, frequently limited human data may be available on a parenteral experimental formulation. In these two previous cases, that is the value listed in Tables I, II, III, and IV. Where only oral human data are available, the authors used their best judgment in correcting the value with a bioavailability parameter. Lowering the cutoff to 70% obviates in most cases any error that would be inherent in classification based on this assumption. However, the criterion for poor metabolism in BDDCS is excretion of unchanged drug both in the urine and in the bile. The extent of biliary excretion of unchanged drug is an experimentally difficult value to obtain in humans for most drugs. But this is the criterion that we have used in the assignment of BDDCS classification for the more than 900 drugs listed in the tables. It will be obvious in reviewing Tables III and IV that a number of class 3 and class 4 compounds show very low values for %Urine. For example, erythromycin is listed in Table III with 4% excreted unchanged in the urine; however, only 15% of an erythromycin dose is metabolized with more than 80% excreted unchanged in the bile. Thus, for the class 1 and 2 drugs in Tables I and II, the low percent urine does reflect fairly accurately the degree of metabolism since for these compounds it is usually the metabolites that are excreted into the bile, not the parent drug. However, for the class 3 and the class 4 compounds, the assignment was not made based only on the percent urine data value in Tables III and IV. The box plot depicted in Fig. 4 reflects these differences between classes 1 and 2 *versus* classes 3 and 4, with the very wide standard deviations below the mean for classes 3 and 4 reflecting the importance of biliary excretion in these assignments.

As mentioned earlier, Benet *et al.* (2) proposed that ≥90% metabolism could be an additional criterion that regulatory agencies may use in confirming that a drug was more than 90% absorbed. In that paper, Benet *et al.* (2) restricted the metabolic processes to those that would only occur following absorption such as cytochrome P450 metabolism or metabolism by phase II enzymes found in the gut or the liver. However, in the present compilation, the metabolism criterion for BDDCS assignment does not limit the metabolic processes to these enzymes only. In the present tables, when a drug is metabolized 70% or more, it is classified as highly metabolized and if the metabolism is <70% is categorized as poorly metabolized (readers will note in Fig. 4 that five class 1 and 2 drugs show between >30% and ≤40% excreted unchanged. For these compounds, it is the authors' belief that these drugs operate more like the assignment made).

Maximum Strength Dose

For US-approved drugs, the maximum dose strength is taken from the package insert. In a number of cases, we have included drugs in the tables that have been removed from the market and drug products where a package insert was not available. In those cases, the maximum strength dose was selected based on an evaluation of literature data.

Figure 5 is a box plot of the −Log10 of the maximum strength dose (molar) against BDDCS. It appears that class 4 drugs have the highest dose (molar) compared with other BDDCS classes, whereas class 1 drugs have the lowest strength. This most likely relates to differences in bioavailability, but may also relate to differences in efficacy. The more lipophilic highly metabolized drugs tend to be more active toward wanted and off targets because of a higher capability of nonspecific interactions. Therefore, it is more likely that drugs that are less lipophilic and less metabolized are given at a higher dose since they are probably less potent and since there is less risk of toxicity.

BDDCS Classification and Dose Number

High *versus* low solubility was determined using the FDA/EMA criteria of the maximum strength dose of the drug at its lowest solubility over the pH range of 1–7.5 being soluble in 250 mL of water at 37°C. The solubility cutoff may be expressed as the dose number, which is calculated as the highest dose strength (milligrams) divided by 250 mL and the lowest solubility (milligrams per milliliter). When the dose number is ≤1.0, the drug is considered to have high solubility; when the dose number is >1.0, the drug is considered to have low solubility. Using the solubility (dose number) and the

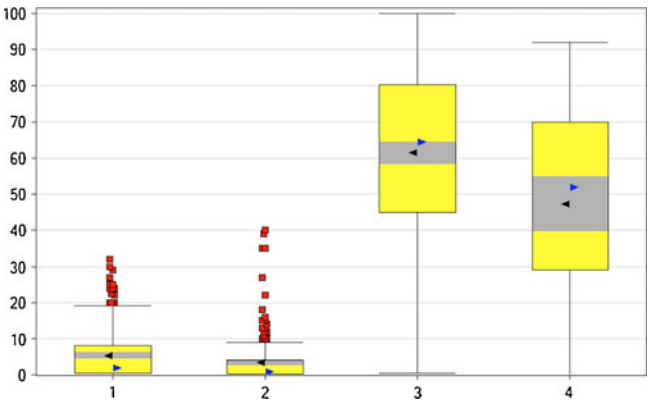

Fig. 4. Box plot of%Urine against BDDCS. Key: as in Fig. 3. Class 1, 5.3±6.8 (302); class 2, 3.5±6.3 (228); class 3, 61.3±24.4 (243); class 4, 47.8±27.1 (50)

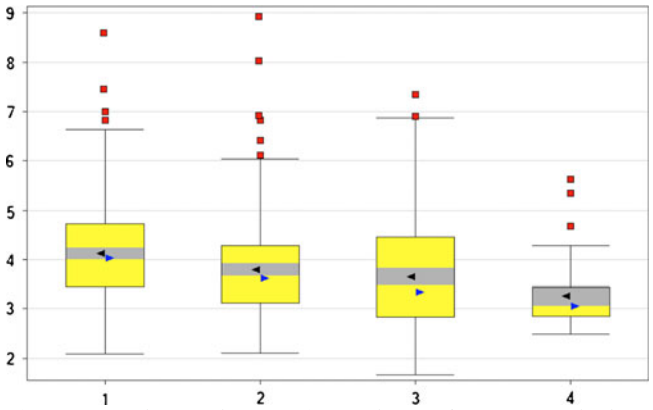

Fig. 5. Box plot of the −Log10 of the maximum strength dose (molar) against BDDCS. Key: as in Fig. 3. Class 1, 4.12±1.01 (288); class 2, 3.79±0.98 (237); class 3, 3.67±1.13 (163); class 4, 3.24±0.69 (43)

percent metabolism criteria discussed above, the BDDCS class was assigned. For non-orally dosed drugs and active metabolites, no dose number is given in the tables, and the BDDCS assignment is based on the best estimate of the relevant solubility as determined by the authors. This opens the possibility of a more refined system, the dose-dependent BDDCS, dBDDCS. Such a system, based on evaluating multiple strength doses, could highlight "class migration," which is likely to occur for some drugs, *versus* "class propensity." We anticipate that some drugs will migrate to a neighboring class depending on dose strength, whereas most drugs, however, are likely to show preference for one class only. By migrating existing class 4 drugs toward class 3 or class 2 drugs toward class 1, one is likely to obtain improved biopharmaceutical characteristics; thus, FDA approval for novel formulations can be requested using a drug repurposing mechanism (36) under Section 505(b) (2) of the Federal Food, Drugs and Cosmetic Act.

Class Zero

For a number of drugs, such as amphetamine, changes in urinary pH affect the extent of metabolism. Therefore, it is not possible to assign a BDDCS class. It appears for the 11 drugs listed in Table V that they all are predominantly highly soluble in water and thus would probably be BCS class 1 drugs, or BDDCS class 1 or class 3 depending upon urine pH.

MLog*P* and MLog$D_{7.4}$

When no active transport processes are involved, pharmaceutical scientists expect lipid/water partition coefficients to be correlated with drug permeability. The Lipinski Rule of Five (37–39) was an attempt to define the upper limits of lipophilicity for developing NMEs that are likely to be orally available. As noted above, Takagi *et al.* (3) evaluated the correlation of measured Log*P* and calculated Log*P* with BCS high *versus* low human jejunal permeability rate compounds, finding that the correlation only held about two thirds of the time. Since there is interest in these parameters and following our guideline of attempting to use measured experimental values when available in making predictions, we have included in Tables I, II, III, IV, and V values for measured Log*P* and measured Log*D* at pH 7.4 when such values are available. Again, individual references for the values are not included. However, in the section below, we will comment on prediction differences and accuracy with respect to *in silico* calculations. Figure 6 is a box plot of the measured Log*D* values at pH 7.4 against BDDCS assignment.

This provides some partial explanation for the food effects mentioned earlier. BDDCS class 2 drugs have high-fat solubility, as illustrated by their higher measured Log$D_{7.4}$ (Fig. 6), compared with other classes. Under high-fat meal conditions, higher amounts of drug are therefore likely to be solubilized in the intestinal contents and become available to the enterocytes for (passive) absorption. However, we do not see a similar effect for the more hydrophilic, poorly soluble class 4 drugs. Since BDDCS class 1 drugs already are solubilized, they would receive no benefit from increased lipid solubilization.

IN SILICO PARAMETERS

As discussed above, BDDCS assignments were based on the measured parameters of extent of metabolism and solubility, although in the latter case, for extremely poorly soluble and very highly soluble compounds, a numerical value is not always available. However, it is also useful to analyze how well or how poorly *in silico* parameters can predict the BDDCS classification and to use this type of computation to make other predictions. Thus, for each compound in the tables, we also include: the molecular weight of the listed compound; the calculated Log*P* (CLog*P*) using the method of Leo (40); the number of hydrogen bond donors (HDo) for the active moiety; the number of hydrogen bond acceptors (HAc) for the active moiety; the polar surface area (PSA) calculated using the method of Clark (41); and the log of the lowest water solubility calculated over the pH range 3–7.5 (minVSLgS; VolSurf+), as proposed by Cruciani *et al.* (42,43). We also calculated (and list in Supporting Info) the solubility of each drug in its neutral form using Tetko's solubility in water (TLogS_w) prediction using ALOGPS 2.1 [see (44)]. We hope that this parameter compilation and discussion will be valuable to investigators trying to develop better prediction methods.

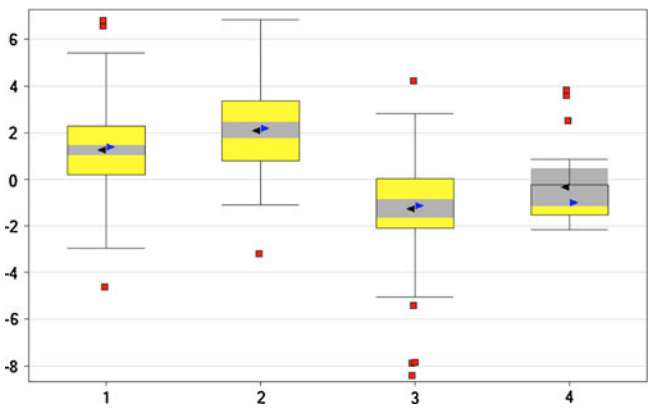

Fig. 6. Box plot of MLog$D_{7.4}$ values against BDDCS. MLog$D_{7.4}$ for class 2, 2.09±1.91 (121) is the highest among all classes. Class 1, 1.25±1.68 (219); class 3, −1.26±2.19 (110); and class 4 −0.42±1.77 (20). Key: as in Fig. 3

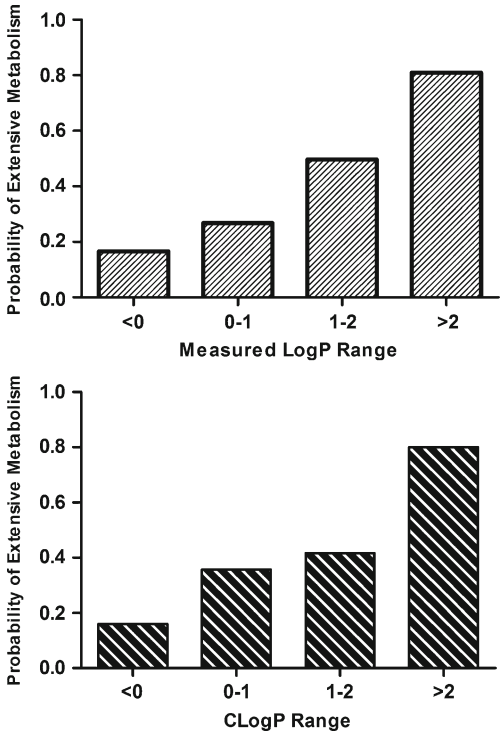

Fig. 7. Probability of extensive metabolism in different measured Log*P* and CLog*P* ranges. The plot show the probability of being extensively metabolized in a specific Log*P* (CLog*P*) range if a set with equal number of extensively and poorly metabolized drugs is considered

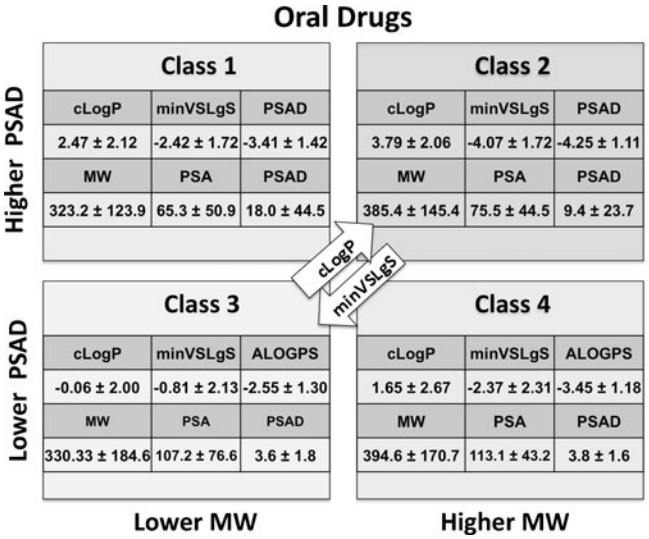

Fig. 8. *In silico* parameters for 698 orally dosed drugs. For each, calculated property average value and standard deviation are shown. PSAD (polar surface area density) = MW/PSA

Solubility and Dose Number

Both *in silico* solubility predictions correlate poorly with the measured values, although the VolSurf+ correlation (r^2=0.33) is somewhat better than the ALOGPS solubility (r^2=0.24). However, even with these poor correlations, the predicted dose numbers (cDose Number) with the calculated VolSurf+ solubility were reasonable for class 1, 2, and 3 drugs. Results for the VolSurf+ (and ALOGPS) solubilities were as follows: Class 1 drugs are classified with an accuracy of 78.6% (54.3%), class 2 with an accuracy of 76.9% (84.3%), and class 3 with accuracy of 89.4% (65.7%). The predictive accuracy for class 4 drugs was very poor (39.5%) for the VolSurf+ prediction, but reasonable when the pH effect is not considered (79.1% when using ALOGPS). Upon further examination, 17 of these drugs are well predicted by cDose Number. These 17 drugs have a "class2-like" CLog*P* profile (average CLog*P*=3.76). The deviation between measured Log*S* and minVSLgS is on average 0.66 for these drugs. For the 26 class 4 drugs that are poorly predicted, the average CLog*P* is 0.27, and the average measured Log*P* is 0.11. The deviation between measured Log*S* and minVSLgS is on average around 3.00. A number of these 26 drugs are likely to exist as zwitterions at pH below 7.5; several among them are fluoroquinolone antibiotics. In particular, for enoxacin, ciprofloxacin, norfloxacin, and cinoxacin, solubility prediction based on melting point and Log*D* failed, probably due to self-association (45). In support of this hypothesis, Ross and Riley (45) noted that the solubility of these drugs at the same pH increases with temperature. The lowest measured solubility data for class 4 drugs are observed when these molecules behave as zwitterions (pH 7). Therefore, the reason for class 4 assignment prediction error is likely to relate to self-association for drugs that behave as zwitterions. This is less likely to play a role in the digestive tract since varying pH conditions, the presence of counterions, and surfactants (*e.g.*, bile acids) might diminish the importance of self-association. Despite the relatively high success of the ALOGPS method for class 4, solubility predictions for these zwitterions in neutral form, which essentially ignores the pH effect, should be used with caution.

Partition Coefficient and Extent of Metabolism

As discussed above, a high extent of metabolism is expected for high Log*P* compounds and *vice versa*. In contrast to the predicted *versus* measured solubility values discussed above, the correlation between MLog*P* *versus* CLog*P* is quite good (r^2=0.83). Thus, it might be expected that both MLog*P* and CLog*P* would reasonably well predict

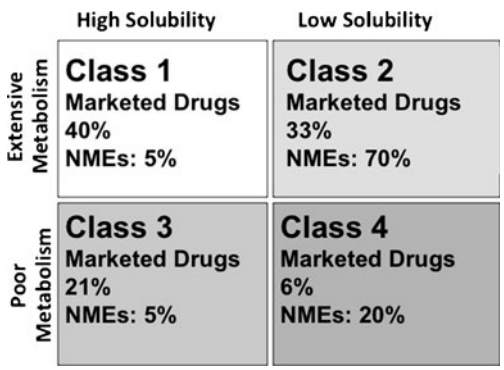

Fig. 9. BDDCS distribution of 698 marketed, immediate release, orally dosed drugs in the present table *versus* the predicted distribution of small molecule NMEs being developed by the industry

class 1 and 2 drugs *versus* class 3 and 4 drugs, with the results shown in Fig. 7. For either measured or calculated Log*P*>2, the probability of extensive metabolism is 80.1% and 79.3%, respectively. For Log*P* values<0, the probability of poor metabolism is 83.5% for MLog*P* and 83.9% for CLogP. However, when Log*P* values range from 0 to 2 (31.7% of drugs for MLog*P* and 27.5% of drugs for CLog*P*), the probability assignments are not very good, with MLog*P* doing somewhat better for extensively metabolized drugs and CLog*P* doing somewhat better for poorly metabolized drugs (Fig. 7). As with solubility predictions, the poorest probability of extent of metabolism was found for class 4 drugs (data not shown).

Summary of *In Silico* Parameters for Orally Dosed Drugs

Figure 8 highlights the *in silico* parameters for 698 orally dosed drugs. As expected, CLog*P* is higher and PSA lower for extensively metabolized (class 1 and 2) drugs. However, an unexpected finding is the very marked similarity for solubility and (somewhat less) for CLog*P* predictions for class 1 and 4 drugs. This reflects the inherent confounding aspects of the dose number calculation used in both BDDCS and BCS, as discussed earlier in this manuscript and by Rinaki *et al.* (46), and the generally poor predictability for class 4 drugs. We also calculated the polar surface area density (PSAD = MW/PSA) and are struck by the empirical observation of the similarity and low coefficient of variation for PSAD (Fig. 8) for the class 3 and class 4 poorly metabolized drugs. As noted by the arrows in Fig. 8, class 2 and class 3 drugs exhibit the extremes for the *in silico* measures of solubility and partition coefficient.

OTHER COMMENTS

The listing of drugs in the five tables is essentially inclusive of small molecules only as most peptide and protein drugs were not included in the compilation. However, there are exceptions, such as the inclusion of exenatide and liraglutide. We note that all the drugs listed in the 2011 Goodman and Gilman compilation (47) are included in the present table except, for streptokinase and interferon alpha and beta. Since many drugs on the market are in fact prodrugs, when data were available, our listing includes the parameters for some of the better characterized active metabolites, even when the metabolite itself was not a commercially available product and thus the maximum strength dose does not exist. For example, see flurazepam and desalkylflurazepam (both Table I) as well as losartan (Table II) and EXP3174 (Table III). In those cases, the BDDCS classification was made based on the dose of the parent drug, the known fraction conversion to the active species, and the solubility of the active metabolite. The finding of Wu and Benet (1) that very few drugs fall in the 30–70% metabolism range does not mean that there are no such drugs. For example, in Table III, moxifloxacin HCl has been shown to be metabolized 52% (14% as a glucuronide and 38% as a sulfate conjugate) while 45% is excreted unchanged (25% in the feces and 20% in the urine). Similarly, palonosetron HCl (Table III) is excreted 40% unchanged and 50% via CYP enzymes, while phenazopyridine (Table IV) is excreted 41% unchanged and 49% metabolized.

WHERE CAN ADDITIONAL INFORMATION BE FOUND?

Oprea and co-workers (48,49) have indexed the information for over 1,260 drugs in WOMBAT-PK, a database that includes pharmacokinetic parameters (such as those indexed in Goodman–Gilman), physicochemical properties, and target bioactivities (see http://www.sunsetmolecular.com/index.php?option=com_content&view=article&id=16&Itemid=11). WOMBAT-PK contains additional information related to the BDDCS entries described in the tables. However, all pertinent data used to categorize individual drugs for the BDDCS classification are provided here. Further information about drugs can also be found in public resources as follows: Chemical information, physicochemical properties, and bioactivities are compiled in PubChem (http://pubchem.ncbi.nlm.nih.gov/), ChEMBL (https://www.ebi.ac.uk/chembl/), and ChemSpider (http://www.chemspider.com/). Detailed drug information can be retrieved at DailyMed (http://dailymed.nlm.nih.gov/dailymed/about.cfm), DrugBank (http://drugbank.ca/), and European Medicines Agency (http://www.ema.europa.eu/).

Information as found in the five tables, together with the physicochemical properties and target bioactivities, can serve as a source for investigating and predicting the characteristics of NMEs in drug development. However, we add a further caution concerning *in silico* methodologies that may be developed based on our compilation of data for drugs on the market at some time. This is illustrated in Fig. 9 where we have compiled the BDDCS classification of the orally dosed drugs in our tables. In Fig. 9, we compare this distribution of commercially available drugs with our predictions of the distribution of total NMEs that have at some time been dosed to humans, particularly in the last decade. Based on our prior evaluation of high-activity medicinal chemistry compounds (50), we estimate that of the drug candidates being investigated by the industry, up to 70% are large molecular weight, lipophilic, poorly soluble class 2 compounds, another 20% are not only poorly soluble but also poorly permeable class 4 compounds, while only 10% are high-soluble class 1 and class 3 compounds. Thus, when *in silico* methodologies are developed and tested on commercially available drugs, it is important to remember that 40% of drugs are BDDCS class 1, and as predicted in Fig. 2, these compounds will not exhibit disposition characteristics affected by transporters in the gut and liver, whereas up to 95% of NMEs are likely to be affected. Therefore, in testing such new methodologies, it is critical that both the training and test compound sets have a strong representation of compounds other than BDDCS class 1.

ACKNOWLEDGMENTS

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Supporting Info Available An excel file is available as supporting info containing the following data for the 927 drugs dataset: name, BDDCS class, max dose strength value, max dose strength unit, formulation, route, measured solubility, dose number, % excreted unchanged in urine, MW drug, MW solution, pDose, measured LogS molar, measured LogP, measured $LogD_{7.4}$, ALOGPS 2.1 solubility, cDose Number (ALOGPS based), minVSLgS, cDose Number (minVSLgS based), cLogP, HBA,HBD, PSA, and violations to Rules of Five. Definitions for the terms used only in the supporting info file may be found at the end of that data set. In addition, box plots of minVSLgS, ALOGPS 2.1 solubility, MLogP, cLogP, MW, PSA parameters against BDDCS are provided.

REFERENCES

1. Wu C-Y, Benet LZ. Predicting drug disposition via application of BCS: transport/absorption/elimination interplay and development of a biopharmaceutics drug disposition classification system. Pharm Res. 2005;22:11–23.
2. Benet LZ, Amidon GL, Barends DM, Lennernäs H, Polli JE, Shah VP, *et al*. The use of BDDCS in classifying the permeability of marketed drugs. Pharm Res. 2008;25:483–8.
3. Takagi T, Ramachandran C, Bermejo M, Yamashita S, Yu LX, Amidon GL. A provisional biopharmaceutical classification of the top 200 oral drug products in the United States, Great Britain, Spain and Japan. Mol Pharmaceut. 2006;3:631–43.
4. Food and Drug Administration. Guidance for industry: waiver of *in vivo* bioavailability and bioequivalence studies for immediate-release solid oral dosage forms based on a biopharmaceutics classification system. Food and Drug Administration, Rockville, MD. 2000. www.fda.gov/cder/guidance/index.htm.
5. Amidon GL, Lennernäs H, Shah VP, Crison JR. A theoretical basis for a biopharmaceutics drug classification: the correlation of *in vitro* drug product dissolution and *in vivo* bioavailability. Pharm Res. 1995;12:413–20.
6. Benet LZ, Larregieu CA. The FDA should eliminate the ambiguities in the current BCS biowaiver guidance and make public the drugs for which BCS biowaivers have been granted. Clin Pharmacol Ther. 2010;88:405–7.
7. Chen ML, Amidon GL, Benet LZ, Lennernäs H, Yu LX. The BCS, BDDCS and regulatory guidances. Pharm Res. 2011;28:1774–8.
8. Lennernäs H. Intestinal permeability and its relevance for absorption and elimination. Xenobiotica. 2007;37:1015–51.
9. European Medicines Agency. Guideline on the investigation of bioequivalence. Doc. Ref.:CPMP/EWP/QWP/1401/98 Rev.1/Corr. http://www.ema.europa.eu/pdfs/human/qwp/140198enrev1fin.pdf. Accessed 28 March 2010.
10. Chen ML, Yu L. The use of drug metabolism for prediction of intestinal permeability. Mol Pharmaceut. 2009;6:74–81.
11. Fraga S, Pinho MJ, Soares-da-Silva P. Expression of LAT1 and LAT2 amino acid transporters in human and rat intestinal epithelial cells. Amino Acids. 2005;29:229–33.
12. Lyrica™ package insert. http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=42134#nlm34090-1.
13. Shugarts S, Benet LZ. The role of transporters in the pharmacokinetics of orally administered drugs. Pharm Res. 2009;26:2039–54.
14. Matthews EJ, Krulak NL, Benz RD, Contrera JF. Assessment of the health effects of chemicals in humans: I. QSAR estimation of the maximum recommended therapeutic dose (MRTD) and no effect level (NOEL) of organic chemicals based on clinical trial data. Curr Drug Discov Technol. 2004;1:61–76.
15. Benet LZ. The drug transporter-metabolism alliance: uncovering and defining the interplay. Mol Pharmaceut. 2009;6:1631–43.
16. Benet LZ. Predicting drug disposition via application of a biopharmaceutics drug disposition classification system. Basic Clin Pharmacol Toxicol. 2010;106:162–7.
17. Benet LZ, Cummins CL, Wu C-Y. Transporter-enzyme interactions: implications for predicting drug–drug interactions from *in vitro* data. Curr Drug Metab. 2003;4:393–8.
18. Fleischer D, Li C, Zhou Y, Pao LH, Karim A. Drug, meal and formulation interactions influencing drug absorption after oral administration, clinical implications. Clin Pharmacokinet. 1999;36:233–54.
19. Custodio JM, Wu C-Y, Benet LZ. Predicting drug disposition, absorption/elimination/transporter interplay and the role of food on drug absorption. Adv Drug Deliv Rev. 2008;60:717–33.
20. Wu C-Y, Benet LZ. Disposition of tacrolimus in isolated perfused rat liver: influence of troleandomycin, cyclosporine, and GG918. Drug Metab Dispos. 2003;31:1292–5.
21. Lau Y, Huang Y, Frassetto L, Benet LZ. Effect of OATP1B transporter inhibition on the pharmacokinetics of atorvastatin in healthy volunteers. Clin Pharmacol Ther. 2007;81:194–204.
22. Zheng HX, Huang Y, Frassetto Y, Benet LZ. Elucidating rifampin's inducing and inhibiting effects on glyburide pharmacokinetics and blood glucose in healthy volunteers: unmasking the differential effects of enzyme induction and transporter inhibition for a drug and its primary metabolite. Clin Pharmacol Ther. 2009;85:78–85.
23. Lau YY, Okochi H, Huang Y, Benet LZ. Multiple transporters affect the disposition of atorvastatin and its two active hydroxy metabolites: application of *in vitro* and *ex situ* systems. J Pharmacol Exp Ther. 2006;316:762–71.
24. Lau YY, Okochi H, Huang Y, Benet LZ. Pharmacokinetics of atorvastatin and its hydroxy metabolites in rats and the effects of concomitant rifampicin single doses: relevance of first-pass effect from hepatic uptake transporters, and intestinal and hepatic metabolism. Drug Metab Dispos. 2006;34:1175–81.
25. Frymoyer A, Shugarts S, Browne M, Wu AH, Frassetto L, Benet LZ. Effect of single-dose rifampin on the pharmacokinetics of warfarin in healthy volunteers. Clin Pharmacol Ther. 2010;88:540–7.
26. Sussman NL, Waltershied M, Butler T, Cali JJ, Riss T, Kelly JH. The predictive nature of high throughput toxicity screening using a human hepatocyte cell line. Cell Notes. 2002;3:7–10.
27. Wadelius M, Sorlin K, Wallerman O, Karlsson J, Yue Q-Y, Magnusson PKE, *et al*. Warfarin sensitivity related to CYP2C9, CYP3A5, ABCB1 (MDR1) and other factors. Pharmacogenomics J. 2004;4:40–8.
28. Oprea TI, Tropsha A, Faulon J-L, Rintoul MD. Systems chemical biology. Nature Chem Biol. 2007;3:447–50.
29. Oprea TI, May EE, Leitão A, Tropsha A. Computational systems chemical biology. Meth Mol Biol. 2011;672:459–88.
30. Khandelwal A, Bahadduri PM, Chang C, Polli JE, Swaan PW, Ekins S. Computational models to assign biopharmaceutics drug disposition classification from molecular structure. Pharm Res. 2007;24:2249–62.
31. Willmann S, Schmitt W, Keldenich J, Lippert J, Dressman JB. A physiological model for the estimation of the fraction dose absorbed in humans. J Med Chem. 2004;47:4022–31.
32. Zhao YH, Le J, Abraham MH, Hersey A, Edershaw PJ, Luscombe CN, *et al*. Evaluation of human intestinal absorption data and subsequent derivation of a quantitative structure–activity relationship (QSAR) with the Abraham descriptors. J Pharm Sci. 2001;90:749–84.
33. Meylan MW, Howard PH, Boethling RS. Improved method for estimating water solubility from octanol water partition coefficient. Environ Toxicol Chem. 1996;15:100–6.
34. Yazdanian M, Briggs K, Jankovsky C, Hawi A. The "high solubility" definition of the current FDA Guidance on Biopharmaceutical Classification System may be too strict for acidic drugs. Pharm Res. 2004;21:293–9.
35. Rinaki E, Dokoumetzidis A, Valsami G, Macheras P. Identification of biowaivers among class II drugs: theoretical justification and practical examples. Pharm Res. 2004;21:1567–72.
36. Oprea TI, Nielsen SK, Ursu O, Yang JJ, Taboureau O, Mathias SL, *et al*. Associating drugs, targets and clinical outcomes into an integrated network affords a new platform for computer-aided drug repurposing. Mol Inf. 2011;30:100–11.
37. Lipinski CA, Lombardo F, Dominy BW, Feeney PJ. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Adv Drug Deliv Rev. 2001;46:3–26.
38. Lipinski CA. Drug-like properties and the causes of poor solubility and poor permeability. J Pharmacol Toxicol Methods. 2000;44:235–49.

39. Lipinski CA. Chris Lipinski discusses life and chemistry after the Rule of Five. Drug Discov Today. 2003;8:12–6.
40. Leo AJ. Calculating log *P*oct from structures. Chem Rev. 1993;93:1281–306.
41. Clark DE. Rapid calculation of polar molecular surface area and its application to the prediction of transport phenomena. 1. Prediction of intestinal absorption. J Pharm Sci. 1999;88:807–14.
42. Cruciani G, Crivori P, Carrupt P-A, Testa B. Molecular fields in quantitative structure–permeation relationships: the VolSurf approach. TheoChem-J Mol Struc. 2000;503:17–30.
43. The VolSurf + program, version 1.0.4 is distributed by Molecular Discovery Ltd. http://www.moldiscovery.com.
44. Tetko IV. Computing chemistry on the web. Drug Discov Today. 2005;10:1497–500.
45. Ross DL, Riley CM. Aqueous solubilities of some variously substituted quinolone antimicrobials. Int J Pharmaceutics. 1990;63:237–50.
46. Rinaki E, Valsami G, Macheras P. Quantitative biopharmaceutics classification system: the central role of dose/solubility ratio. Pharm Res. 2003;20:1917–25.
47. Thummel KE, Shen DD, Isoherranen N. Design and optimization of dosage regimens: pharmacokinetic data. In: Brunton L, Chabner B, Knollman B, editors. Goodman and Gilman's the pharmacological basis of therapeutics, vol. 12th. New York: McGraw-Hill; 2011. p. 1891–990 (Appendix II).
48. Olah M, Rad R, Ostopovici L, Bora A, Hadaruga N, Hadaruga D, *et al*. WOMBAT and WOMBAT-PK: bioactivity databases for lead and drug discovery. In: Schreiber SL, Kapoor TM, Wess G, editors. Chemical biology: from small molecules to systems biology and drug design. Weinheim: Wiley-VCH; 2007. p. 760–86.
49. Tetko IV, Oprea TI. Early ADME/T predictions: toy or tool? In: Varnek A, Tropsha A, editors. Chemoinformatics: an approach to virtual screening. London: Royal Society of Chemistry; 2008. p. 240–67.
50. Oprea TI. Current trends in lead discovery: are we looking at the appropriate properties? J Comput Aided Mol Design. 2002;16:325–34.