Prediction of Biopharmaceutical Drug Disposition Classification System (BDDCS) by Structural Parameters

Yeganeh Golfar¹,², Ali Shayanfar³

¹ Biotechnology Research Center, Tabriz University of Medical Sciences, Tabriz, Iran. ² Student Research Committee and Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran. ³ Pharmaceutical Analysis Research Center and Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran

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ABSTRACT - Modeling of physicochemical and pharmacokinetic properties is important for the prediction and mechanism characterization in drug discovery and development. Biopharmaceutics Drug Disposition Classification System (BDDCS) is a four-class system based on solubility and metabolism. This system is employed to delineate the role of transporters in pharmacokinetics and their interaction with metabolizing enzymes. It further anticipates drug disposition and potential drug-drug interactions in the liver and intestine. According to BDDCS, drugs are classified into four groups in terms of the extent of metabolism and solubility (high and low). In this study, structural parameters of drugs were used to develop classification-based models for the prediction of BDDCS class.

Reported BDDCS data of drugs were collected from the literature, and structural descriptors (Abraham solvation parameters and octanol–water partition coefficient (log P)) were calculated by ACD/Labs software. Data were divided into training and test sets. Classification-based models were then used to predict the class of each drug in BDDCS system using structural parameters and the validity of the established models was evaluated by an external test set.

The results of this study showed that log P and Abraham solvation parameters are able to predict the class of solubility and metabolism in BDDCS system with good accuracy. Based on the developed methods for prediction solubility and metabolism class, BDDCS could be predicted in the correct with an acceptable accuracy.

Structural properties of drugs, i.e. logP and Abraham solvation parameters (polarizability, hydrogen bonding acidity and basicity), are capable of estimating the class of solubility and metabolism with an acceptable accuracy.

INTRODUCTION

A major stage in drug discovery and development is evaluating the pharmacokinetic (PK) and physicochemical (PC) properties of the candidate drugs. Computational methods have become an increasingly important part of drug design and discovery over the recent decades, used for predicting the PK and PC of a candidate drug through the use of structural parameters and their correlation which is required for an efficient use of existing drugs and effective development of new drugs [1, 2].

The important parameters which control the rate and extent of oral drug absorption are the drug solubility and gastrointestinal permeability. The importance of these two properties has been emphasized in the biopharmaceutics classification system (BCS) that categorizes drugs into four groups based on their solubility and permeability. In this system, a drug substance is “highly soluble” when its highest dose strength is soluble in 250 mL or less of aqueous media over a pH range of 1-7.5 at 37°C. A drug is “highly permeable” when the extent of absorption in humans is equal or greater than 90% of an administered dose [3, 4].

In 2005, Wu and Benet introduced a new system according to solubility and metabolism, to predict potential drug-drug interactions in the intestine and/or liver and drug disposition. They named this system the biopharmaceutics drug disposition classification system (BDDCS) [5]. Table 1 illustrated the BCS and BDDCS classification of drugs based on solubility and permeability/metabolism.

For class 1 drugs, only metabolic interactions need to be considered in the intestine and the liver. The efflux transporter, metabolic and the efflux transporter-enzyme interaction in the intestine must be taken into consideration for class 2 drugs.

Corresponding Author: Ali Shayanfar, Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran. Email: shayanfara@tbzmed.ac.ir
Table 1. BCS and BDDCS classification of drugs based on solubility and permeability/metabolism.

| Class I     | Class II     | Class III    | Class IV     |
|-------------|--------------|--------------|--------------|
| High solubility | Low solubility | High solubility | Low solubility |
| BCS          | BDDCS        | BCS          | BDDCS        |
| High Permeability | Extensive metabolism | Low Permeability | Low metabolism |

Uptake transporter, efflux transporter and uptake-efflux transporter interaction are of major importance in class 3 and 4 drugs. Therefore, the major route of elimination for class 1 and 2 drugs is metabolism, while that of class 3 and 4 drugs is renal and biliary excretion of unchanged drug [6].

The aim of BDDCS is for characterizing disposition of new molecular entities (NME) and drugs already on the market and the purpose of BCS is to render the bio waivers of in vivo bioequivalence studies facile for drugs that display no significant intestinal absorption problems [7]. Although the classification between BCS and BDDCS only differ about 5-10%, Benet et al. [8] estimated the difference between BCS and BDDCS to occur for about 40% of class 1 drugs, for which FDA has granted bio waivers. Accordingly, knowing the different BDDCS classes based on the structure of a new NME can anticipate its disposition and may reduce the cost of drug discovery and development. Various classification models have been proposed to predict the physicochemical and pharmacokinetic toxicity properties of pharmaceuticals [9-11]. Logistic regression [12, 13] is a simple method and an extension of linear regression and a statistical method used to estimate the relationship between the independent variables in modeling the binary response data.

The purpose of the present research was to predict the class of a drug in BDDCS system. Therefore, the structural parameters of drugs and classification-based models were used to predict solubility and metabolism classes (high or low), separately. Then, these models were applied to estimate BDDCS class.

**COMPUTATIONAL METHODS**

**Processing metabolism and solubility data and calculation of molecular descriptors**

**Data and molecular descriptors**

Experimental classification of 927 drugs based on BDDCS (metabolism and solubility) and corresponding maximum dose of each compound were taken from the published data set of Benet and coworkers [8]. A data set of 595 orally administered drugs from which their highest dose strength expressed as a mass quantity, not as a concentration (e.g. solutions), were included for metabolism and solubility modeling following the removal of all salt forms. For all 595 compounds, SMILES (simplified molecular-input line-entry system) code was employed via www.pubchem.ncbi.nlm.nih.gov, and the numerical values for clogP (calculated octanol–water partition coefficient) and Abraham solvation parameters were computed by ACD/Labs software (https://ilab.acdlabs.com). These parameters are independent variables, or descriptors, with the following solute properties: E is the excess molar refraction, S indicates dipolarity/polarizability descriptors of the solute, A and B are the solute hydrogen-bond acidity and basicity, and V is the McGowan volume of the solute [14].

**Classification of data to training and test sets**

Dataset was sorted based on ascending clogP, where from six consecutive compounds, one was allocated to the test set. The training sets were used to build separate models and predict metabolism and solubility classes. Therefore, 595 compounds classified into 496 compounds for the training set and the remaining data (99 data points) as test set to evaluate the prediction capability of the developed models.

**Binning of solubility compounds**

496 compounds were divided into the following groups:

1) Compounds with high solubility (class 1 and 3) according to BDDCS as class H (high solubility).
2) Compounds with low solubility (class 2 and 4) according BDDCS as class L (low solubility).

**Binning of metabolism compounds**

496 compounds were divided into the following groups:

1) Compounds with high metabolism (class 1 and 2) according to BDDCS as class H (high metabolism).
2) Compounds with low metabolism (class 3 and 4) according to reference BDDCS as class L (low metabolism).

**Modeling**

Various thresholds and models developed by the training set (based on the structural parameters, clogP and Abraham solvation parameters) were analyzed, and the optimal parameters and their values were obtained by calculating the prediction accuracy of solubility and metabolism class (number of correct prediction/total data) for the test set. The threshold to define the boundary between high and low metabolism was set at clogP=2. Therefore, a compound with clogP>2 would be defined as high metabolism and a compound with clogP<2 would follow a binary regression model. The definition of the borderline between high and low solubility was set at maximum dose=10 mg, hence compounds with a maximum dose under 10 mg would be defined as highly soluble and those with a maximum dose higher than 10 mg followed a binary logistic regression by SPSS version 21 software (www.spss.com.hk) for classification of drugs into the two mentioned sub-groups.

For the binary regression method, each class (metabolism and solubility) was set as a dependent variable and binary classification was carried out using selected molecular descriptors as independent variables to develop the models for metabolism and solubility. Features were selected for the logistic regression model based on probability values (p-value) associated with each descriptor whenever they were statistically significant at the 99% level (p<0.01). It shows the probability that the descriptor is there by chance is less than 1% [15].

P-values and coefficients in regression analysis work together to show relationships in the model that are statistically significant. The software compares the t-statistic with values in the Student’s t distribution to determine the p-value.

The models were developed by binary logistic regression and structural parameters, clogP and Abraham solvation parameters, and maximum dose to predict BDDCS class. Separate models for metabolism and solubility were built using training sets of 496 compounds. The prediction capability of the developed models was checked by a test set composed of 99 compounds.

**RESULTS**

**Solubility prediction**

In the training set, 20% of the drugs had a maximum dose lower than 10 (N=100). Most of these drugs (85%) belonged to class 1 and 3 (highly soluble), a criterion applied to classify them in the correct group with a good accuracy. Based on the definition, when the highest dose strength of a drug substance is soluble in 250 mL or less of aqueous media over a pH range of 1-7.5 at 37°C, it is considered as “highly soluble”[16]. Therefore, dose is a critical parameter based on the obtained results in this work and most drugs with a maximum dose of 10 mg or less are highly soluble. The remaining data points (N=396) were applied to develop a model by Abraham solvation parameters and clogP based on binary logistic regression, where the obtained model is:

\[
p = \frac{e^{(3.203+1.295B- .8825-0.373clogP)}}{1+e^{(3.203+1.295B- .8825-0.373clogP)}} \quad \text{Eq. 1}
\]

where P is the probability of binary responses (class 0 or 1) based on the solubility. In addition, probability values (p-value) associated with each descriptor were less than 0.01. The model was able to predict (Eq. 1) 79% and 68% of high and low soluble drugs of the training set in the correct group, respectively. Overall, using maximum dose, B (hydrogen bond basicity), S (polarizability) and clogP, the solubility class of 74% of compounds was classified in the correct group.

To evaluate the prediction capability of the model, 99 compounds in test set were used to predict the correct class of drug based on solubility. 82% of the compounds with maximum doses lower than 10 (N=17) were highly soluble, and Eq. 1 could accurately predict 73% of drugs with maximum doses higher than 10 (N=82) in correct group. Therefore, total prediction accuracy for the test set was 74%.

**Metabolism prediction**

In training set, 54% drugs had a clogP higher than 2 (N=270). Most of these drugs (91%) belonged to class 1 and 2 (high metabolism), a criterion applied to classify them in the correct group with a good accuracy. The remaining data points (N=226) were applied to develop a model by Abraham solvation parameters and clogP based on binary logistic regression, where the obtained model is:

\[
p = \frac{e^{(0.734-1.260A+ .357clogP)}}{1+e^{(0.734-1.260A+ .357clogP)}} \quad \text{Eq. 2}
\]

Eq. 2 was able to correctly predict 80% and 66% of high and low metabolize drugs in the correct class, respectively. Generally, using A (hydrogen bond acidity) and clogP, metabolism class of 83%
of the studied drugs could be classified in the correct group.

To evaluate the prediction capability of the model, 99 compounds in the test set were used to predict the correct class of drug based on metabolism. 89% of compounds with clogP higher than 2 (N=54) were high metabolism and Eq. 2 could accurately predict 84% of drugs with clogP lower than 2 (N=45) in the correct group. Overall, total prediction accuracy for the test set was 86%.

**BDDCS prediction**

The results associated with the prediction of the BDDCS class of the studied drugs are shown in Table 2. Based on the developed methods for prediction solubility and metabolism class, 64% and 63% of training and test set could be predicted in the correct BDDCS class.

**DISCUSSION**

In this study, we described a computational method to predict the BDDCS class of compounds based on their molecular descriptors. The dataset was obtained from the published data set of Benet et al. [8]. Due to the removing salts and the solution forms of drugs, the dataset was reduced to 595 oral drugs, divided into training (496 drugs) and test (99 drugs) sets. As outlined earlier, BDDCS is a modification of the BCS [17] that utilizes drug metabolism rather than intestinal permeability [18]. In this work, we attempted to build models to predict the class of metabolism and solubility class.

Both metabolism and solubility are important properties in drug discovery. However, these properties are complex and can be difficult to model. BDDCS class prediction can overcome variable metabolism and solubility data by predicting the compound classes rather than specific values as a primary initial screening of compounds. However, suitable thresholds for discriminating between high and low metabolism/solubility should be carefully considered.

There are many factors influencing solubility and metabolism, where a threshold for discriminating between high and low metabolism/solubility can be used to improve the prediction of BDDCS class. The definition of the borderline between high and low solubility is set at maximum dose 10 mg. Compounds with maximum doses lower than 10 mg were defined as highly soluble (85% and 82% for training and test set, respectively) while only 55% of drugs with maximum dose>10 are high soluble. Therefore, Eq. 1 is necessary for classification of data with a high dose in correct group. Using B, S and clogP (Eq. 1), solubility class could be accurately predicted (74% and 73% for training and test set, respectively) for those with maximum doses of higher than 10. The results for the prediction solubility class of drugs are shown in Figure 1. These data show that maximum dose is necessary for prediction class of solubility.

The optimal threshold to define the boundary between high and low metabolism based on the training set is set at clogP=2. In compounds with clogP higher than 2, metabolism classes were predicted with good accuracy (91% and 89% for training and test set, respectively). In other words, the compounds with clogP>2 are lipophilic compounds with high metabolism. Moreover, the model developed based on logistic regression by clog P and A (Eq. 2) for low metabolism drugs (clogP<2) was able to predict the metabolism class of studied compounds with an acceptable accuracy (73% and 84% for training and test set, respectively). These findings indicate that clogP which used to predict various physicochemical, pharmacokinetic and biological properties of compounds [19-21] and could be calculated based on the structure of compounds with good accuracy [22], is a crucial parameter to predicting the metabolism class of drugs in BDDCS. The intrinsic lipophilicity (log P) is a common parameter for predicting solubility and metabolism. It is a physical feature introduced to describe a compound’s affinity towards lipid-like environments, affecting drug absorption, bioavailability, hydrophobic drug-receptor interactions, and metabolism of molecules. It describes the equilibrium distribution of molecular drug candidates (unionized form of the molecule) between water and octanol and is independent of pH. Several researchers have reported an inverse relationship between clogP and aqueous solubility [23-25]. ClogP has been utilized instead of experimental logP in modeling studies, where there is a high correlation between them [26, 27].

A (hydrogen bond acidity) is yet another significant parameter for predicting the metabolism of low lipophilic drugs clogP<2. The results related to the prediction metabolism class of the studied drugs were shown in Figure 2.

Collinear descriptors (R²>0.8) should be avoided in developing models [28], as they may entail the over fitting of the data. The inter-correlation between the selected parameters in Eq. 1 and 2 was less than 0.5, a value corroborating the validity of the developed model from this viewpoint.
Figure 1. Prediction of solubility class. Number of training set and test sets are 496 and 99, respectively. N is number of compounds.

\[ P = \frac{e^{(3.203+1.295B-1.8825-0.373\text{clog}P)}}{1 + e^{(3.203+1.295B-1.8825-0.373\text{clog}P)}} \]

Figure 2. Prediction of metabolism class. Number of training set and test sets are 496 and 99, respectively. N is number of compounds.
Similar results associated with the prediction of the solubility and metabolism class of external test set confirm the prediction capability of the developed models.

Both models applied the Abraham solvation parameters for the prediction of solubility and metabolism, confirming the previous studies which applied these parameters for the analysis and prediction of physicochemical properties and pharmacokinetic parameters such as adsorption, distribution and toxicological features of drugs [14, 29, 30].

A computational procedure for predicting the BDDCS class was attempted by Broccatelli et al [31] by molecular structures calculated from the VolSurf+ software. Similarly, the proposed method predicted the BDDCS class with relatively good accuracy with a general lack of predictability for class 4 drugs. However, relatively simple statistical method (logistic regression) and descriptors i.e. clogP and Abraham solvation parameters of solute, are more acceptable in modeling studies [15], and could be useful in predicting solubility and metabolism class and estimating drug-drug interactions and transporter effects in drug disposition.

Solubility and metabolism are complex parameters whose values are affected by various factors. It is possible that the applied parameters were not sufficient to estimate the correct class. However, the variations and inaccuracy of data are among the possible reasons for the unsuccessful attempts of medicinal chemists in developing models with high capability of predicting the physicochemical, pharmacokinetic and activity of drugs. For instance, the best model for aqueous solubility prediction has a mean percentage deviation (MPD) of more than 100% [32], and the MPD value for solubility in the solvent mixture is higher than 25% for pharmaceuticals [33].

In this study, we demonstrated that the developed models for prediction solubility and metabolism could estimate BDDCS with 64% accuracy, a value which does not seem to be very satisfactory. However, following the publication of BDDCS for over 900 data points in 2011 [8], Benet and coworkers [34] in 2016 amend the classification of 13 drugs. In this data set, five compounds in the training set (colchicine, diclofenac, flecainide, pindolol and saxagliptin) and four compounds in the test set (aliskiren, clonidine, metoclopramide and pitavastatin) were corrected in terms of BDDCS. These data (old and new class, and prediction class in this study) are listed in Table 3. According to the old data set, the proposed method can predict only one compound in the correct group, while based on the updated data, the BDDCS class of five data points (diclofenac, flecainide, metoclopramide, pindolol and clonidine) was classified in the correct group. Given the possible errors in experimental data and maximum 25% prediction based on probability rules, the obtained results confirm the good accuracy of the developed models. Given the possible incorrect errors in experimental data and maximum 25% prediction based on probability rules, the obtained results confirm the good accuracy of the developed models.

CONCLUSION

To predict the BDDCS of compounds, we proposed the use of threshold values by two parameters, clogP for metabolism and maximum dose for solubility, and logistic regression based models using clogP and Abraham solvation parameters.

The descriptors utilized in this work (the three Abraham solvation parameters, namely A, B and S) showing hydrogen bond acidity and basicity, and polarizability, respectively, clogP and maximum dose of compounds are adequate for the prediction of solubility and metabolism, and can be used in the prediction of BDDCS of drugs with an acceptable accuracy.

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Table 2. List of studied compounds, BDDCS class, structural parameters and prediction class of solubility (high=H, low=L), metabolism (high=H, low=L) and BDDCS class by the developed methods in this study (A: hydrogen bond acidity, B: hydrogen bond basicity, S: polarizability, log P: octanol–water partition coefficient)

| No. | Generic Name     | BDDCS | A:  | B:  | S:  | clogP | Dose (mg) | Prediction of solubility | Prediction of metabolism | Prediction of BDDCS |
|-----|------------------|-------|-----|-----|-----|-------|-----------|--------------------------|--------------------------|---------------------|
| 1   | Acarbose         | 1     | 3.35| 6.22| 4.52| -6.66 | 100       | H                        | L                        | 3                   |
| 2   | Acetaminophen    | 1     | 0.95| 0.8 | 1.63| 0.49  | 1000      | H                        | L                        | 3                   |
| 3   | Acetazolamide    | 4     | 0.85| 1.5 | 2.55| -0.98 | 250       | H                        | L                        | 3                   |
| 4   | Acetohexamide    | 1     | 0.59| 1.46| 2.79| 2.25  | 500       | L                        | H                        | 2                   |
| 5   | Acrivastine      | 3     | 0.57| 1.45| 2    | 1.46  | 8         | H                        | H                        | 1                   |
| 6   | Acyclovir        | 4     | 0.65| 2.18| 1.95| -2.42 | 800       | H                        | L                        | 3                   |
| 7   | Adefovir Dipivoxil| 3     | 0.23| 2.91| 2.93| -1.98 | 10        | H                        | L                        | 3                   |
| 8   | Albendazole      | 2     | 0.71| 1.12| 1.96| 3.46  | 200       | L                        | H                        | 2                   |
| 9   | Albuterol        | 3     | 1.19| 1.82| 1.26| 0.06  | 4         | H                        | L                        | 3                   |
| 10  | Aflaminalin      | 1     | 0.63| 1.01| 1.01| 8.24  | 1         | H                        | H                        | 1                   |
| 11  | Allopurinol      | 2     | 0.27| 1.54| 1.04| 0.63  | 300       | H                        | H                        | 1                   |
| 12  | Almotriptan      | 3     | 0.31| 1.65| 2.16| 1.79  | 12.5      | H                        | H                        | 1                   |
| 13  | Alsohexine       | 1     | 0.35| 1.38| 2.64| 1.74  | 1         | H                        | H                        | 1                   |
| 14  | Alprazolam       | 1     | 0.84| 1.95| 2.56 | 2      | H         | H                        | 1                      |
| 15  | Alpranolol       | 1     | 0.29| 1.36| 1.12| -0.86 | 200       | H                        | H                        | 1                   |
| 16  | Altretamine      | 2     | 0   | 1.3 | 1.53| 1.67  | 10        | H                        | H                        | 1                   |
| 17  | Alvimopan        | 3     | 1.33| 1.96| 1.41| 2.16  | 100       | H                        | H                        | 1                   |
| 18  | Amantadine       | 3     | 0.21| 0.64| 0.68| 2     | 100       | H                        | H                        | 1                   |
| 19  | Ambrisentan      | 1     | 0.57| 1.52| 2.32| 3.33  | 10        | L                        | H                        | 2                   |
| 20  | Amboxol          | 1     | 0.73| 1.12| 1.89| 2.66  | 30        | H                        | H                        | 1                   |
| 21  | Amiloride        | 3     | 1.01| 2.16| 2.12| 0.11  | 5         | H                        | L                        | 3                   |
| 22  | Aminogluthethimide| 2     | 0.56| 1.34| 1.79| 0.77  | 250       | H                        | H                        | 1                   |
| 23  | Aminophenazone   | 1     | 0   | 1.79| 1.88| 1.04  | 300       | H                        | H                        | 1                   |
| 24  | Amisulpride      | 4     | 0.5 | 2.18| 3.16| 1.8   | 200       | L                        | H                        | 2                   |
| 25  | Amiodipine       | 1     | 0.36| 2.19| 2.26| 3.43  | 10        | H                        | H                        | 1                   |
| 26  | Amoxapine        | 1     | 0.16| 1.43| 1.68| 3.41  | 150       | H                        | H                        | 1                   |
| 27  | Amoxicillin      | 3     | 1.55| 2.9 | 3.59| -1.87 | 500       | H                        | L                        | 3                   |
| 28  | Ampicillin       | 3     | 1.06| 2.62| 3.01| -1.2  | 500       | L                        | H                        | 3                   |
| 29  | Anastrozole      | 1     | 0   | 1   | 2.38| 1.29  | 1         | H                        | H                        | 1                   |
| 30  | Antipyrine       | 1     | 0   | 1.28| 1.75| -1.79 | 500       | H                        | H                        | 1                   |
| 31  | Aprepitant       | 2     | 0.39| 2.11| 2.49| 4.6   | 10        | L                        | H                        | 2                   |
| 32  | Aripiprazole     | 2     | 0.41| 1.75| 2.53| 5.31  | 30        | L                        | H                        | 2                   |
| 33  | Asenapine        | 1     | 0   | 0.91| 1.58| 4.58  | 10        | L                        | H                        | 2                   |
|   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|
| 34 | Astemizole | 2 | 0.13 | 1.64 | 2.7 | 6.09 | 10 | L | H | 2 |
| 35 | Atenolol | 3 | 0.78 | 1.85 | 1.97 | -0.11 | 100 | H | L | 3 |
| 36 | Atomoxetine | 1 | 0.13 | 0.9 | 1.36 | 3.94 | 60 | H | H | 1 |
| 37 | Atovaquone | 4 | 0.31 | 1.21 | 2.54 | 6.35 | 250 | L | H | 2 |
| 38 | Atropine | 3 | 0.31 | 1.31 | 3.15 | 1.3 | 25 | L | H | 2 |
| 39 | Azathioprine | 1 | 0.35 | 1.56 | 2.86 | 0.51 | 100 | L | H | 2 |
| 40 | Azithromycin | 3 | 0.97 | 4.91 | 2.67 | 2.64 | 600 | H | H | 1 |
| 41 | Bambuterol | 1 | 0.38 | 2.25 | 2.2 | 0.56 | 20 | H | H | 1 |
| 42 | Benazepril | 1 | 0.71 | 2.08 | 2.75 | 1.82 | 40 | H | H | 1 |
| 43 | Bendroflumethiazide | 3 | 1.01 | 1.84 | 2.89 | 1.73 | 10 | L | H | 2 |
| 44 | Benidipine | 1 | 0.13 | 2.13 | 2.99 | 7.41 | 8 | H | H | 1 |
| 45 | Benzerazide | 1 | 2.01 | 2.63 | 2.78 | -2.9 | 50 | H | L | 3 |
| 46 | Benznidazole | 1 | 0.35 | 0.57 | 0.98 | 0.9 | 20 | H | H | 1 |
| 47 | Bepridil | 1 | 0 | 1.32 | 1.81 | 6.2 | 400 | L | H | 2 |
| 48 | Beraprost | 1 | 1.2 | 1.51 | 2.03 | 2.04 | 0.04 | H | H | 1 |
| 49 | Betamethasone | 1 | 0.8 | 1.97 | 2.95 | 1.79 | 0.75 | H | H | 1 |
| 50 | Bexarotene | 2 | 0.57 | 0.67 | 1.29 | 8.19 | 75 | L | H | 2 |
| 51 | Bicalutamide | 2 | 0.71 | 1.63 | 3.05 | 2.71 | 50 | L | H | 2 |
| 52 | Biotin | 3 | 0.95 | 1.22 | 1.86 | -0.08 | 5 | H | L | 3 |
| 53 | Biperiden | 1 | 0.31 | 1.17 | 1.32 | 4.94 | 2 | H | H | 1 |
| 54 | Bopindolol | 1 | 0.46 | 1.48 | 2.14 | 4.98 | 2 | H | H | 1 |
| 55 | Bosantan | 2 | 0 | 2.48 | 3.5 | 4.17 | 125 | L | H | 2 |
| 56 | Bromperidol | 1 | 0.31 | 1.45 | 2.16 | 4 | 10 | L | H | 2 |
| 57 | Budesonide | 1 | 0.48 | 2.16 | 3.23 | 2.91 | 3 | H | H | 1 |
| 58 | Bunetanide | 3 | 1.16 | 1.7 | 1.92 | 3.37 | 500 | H | H | 1 |
| 59 | Bupropion | 1 | 0.13 | 0.94 | 1.32 | 3.21 | 100 | H | H | 1 |
| 60 | Buspirone | 2 | 0 | 2.16 | 2.18 | 2.19 | 10 | H | H | 1 |
| 61 | Busulfan | 1 | 0 | 1.46 | 2.25 | -0.59 | 2 | H | H | 1 |
| 62 | Butabarbital | 1 | 0.52 | 1.24 | 1.34 | 1.58 | 100 | H | H | 1 |
| 63 | Butalbital | 1 | 0.52 | 1.3 | 1.4 | 1.63 | 50 | H | H | 1 |
| 64 | Butorphanol | 1 | 0.73 | 1.32 | 1.42 | 3.73 | 5 | H | H | 1 |
| 65 | Cadrilazine | 3 | 0.57 | 1.84 | 2.14 | 0.93 | 10 | H | H | 1 |
| 66 | Caffeine | 1 | 0 | 1.27 | 1.9 | -0.04 | 65 | H | H | 1 |
| 67 | Candesartan cilexetil | 4 | 0.63 | 2.39 | 4.11 | 7.33 | 32 | L | H | 2 |
| 68 | Captopril | 3 | 0.57 | 1.13 | 1.77 | 0.89 | 100 | H | H | 1 |
| 69 | Carbamazepine | 2 | 0.39 | 0.92 | 2.06 | 2.38 | 300 | L | H | 2 |
| 70 | Carbencicillin | 3 | 1.42 | 2.41 | 3.14 | 1.64 | 382 | L | L | 4 |
| 71 | Carbidopa | 1 | 1.69 | 1.77 | 1.79 | -0.45 | 25 | H | L | 3 |
| 72 | Cefaclor | 3 | 1.06 | 2.54 | 3.41 | -1.64 | 500 | H | L | 3 |
| No. | Drug                | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|-----|---------------------|---|---|---|---|---|---|---|---|---|----|
| 73  | Cefadroxil          | 3 | 1.55| 2.82| 3.48| -2.51| 1000 | H | L | 3  |
| 74  | Cefamandole         | 3 | 1.02| 3.18| 2.01| 0.11 | 5    | H | L | 3  |
| 75  | Cefdinir            | 4 | 1.38| 2.85| 3.68| -0.48| 300  | H | L | 3  |
| 76  | Cefditoren Pivoxil  | 2 | 0.5 | 3.45| 4.52| 2.71 | 200  | L | H | 2  |
| 77  | Cefpodoxime        | 4 | 1.07| 2.95| 3.67| -0.41| 200  | H | L | 3  |
| 78  | Cefpodoxime Proxetil| 2 | 0.5 | 3.5 | 1.68| 0.8  | 750  | H | H | 1  |
| 79  | Cefprozil           | 4 | 1.55| 2.89| 3.22| -1.87| 875  | H | L | 3  |
| 80  | Cefributen          | 4 | 1.64| 2.77| 4.02| -1.21| 400  | L | L | 4  |
| 81  | Cefuroxime         | 3 | 1.29| 2.9 | 3.62| 0.23 | 50   | H | L | 3  |
| 82  | Cephradine          | 3 | 1.06| 2.59| 1.06| -1.73| 250  | H | L | 3  |
| 83  | Cervastatin        | 1 | 1.2 | 1.8 | 2.25| 3.56 | 0.8  | H | H | 1  |
| 84  | Cetrizine          | 3 | 0.57| 1.76| 2.24| 2.08 | 5    | H | H | 1  |
| 85  | Chlorambucil       | 1 | 0.57| 0.8 | 1.6 | 3.63 | 2    | H | H | 1  |
| 86  | Chlor Diazepoxide  | 1 | 0.31| 1.41| 1.31| 3.79 | 25   | H | H | 1  |
| 87  | Chloromethiazole   | 1 | 0  | 0.3 | 0.91| 1.68 | 192  | H | H | 1  |
| 88  | Chloroquine        | 3 | 0.13| 1.29| 1.63| 5.06 | 500  | L | H | 2  |
| 89  | Chlorothiazide     | 4 | 0.64| 1.66| 2.74| -1   | 500  | H | L | 3  |
| 90  | Chlorpheniramine   | 1 | 0  | 1.02| 1.49| 3.15 | 4    | H | H | 1  |
| 91  | Chlorpromazine     | 1 | 0  | 0.99| 1.45| 5.3  | 4    | H | H | 1  |
| 92  | Chlorthalidone     | 4 | 1.01| 1.98| 3.05| 0.45 | 100  | L | L | 4  |
| 93  | Chloroxazone       | 2 | 0.45| 0.5 | 1.32| 2.51 | 500  | H | H | 1  |
| 94  | Cilazapril         | 1 | 0.71| 2.51| 2.7 | 0.5  | 2.6  | H | H | 1  |
| 95  | Cilazaprilat       | 3 | 1.28| 2.5 | 2.74| 1.0  | 2.6  | H | H | 1  |
| 96  | Cilostazol         | 2 | 0.41| 1.63| 2.37| 3.53 | 45   | L | H | 2  |
| 97  | Cimetidine         | 3 | 0.74| 1.86| 1.87| 0.19 | 800  | H | L | 3  |
| 98  | Cinoxacin          | 4 | 0.57| 1.55| 2.05| 1.74 | 500  | H | H | 1  |
| 99  | Cisapride          | 2 | 0.5 | 2.17| 3.15| 3.81 | 20   | L | H | 2  |
| 100 | Citalopram         | 2 | 0  | 1.08| 2.25| 3.13 | 20   | L | H | 2  |
| 101 | Clarithromycin     | 3 | 0.8 | 4.49| 2.97| 2.37 | 500  | H | H | 1  |
| 102 | Clavulanic Acid    | 3 | 0.88| 1.79| 1.75| -1.07| 125  | H | L | 3  |
| 103 | Clemastine         | 1 | 0  | 0.97| 1.55| 5.45 | 2    | H | H | 1  |
| 104 | Clodronic Acid     | 4 | 1.25| 2.22| 1.49| -0.14| 800  | H | L | 3  |
| 105 | Clofazimine        | 2 | 0.19| 1.28| 2.34| 7.7  | 50   | L | H | 2  |
| 106 | Clonazepam         | 1 | 0.47| 1.09| 2.25| 2.38 | 2    | H | H | 1  |
| 107 | Cloxicillin        | 4 | 0.84| 2.32| 3.27| 2.52 | 250  | L | H | 2  |
| 108 | Clozapine          | 2 | 0.2 | 1.65| 1.66| 3.71 | 100  | H | H | 1  |
| 109 | Colchicine         | 1 | 0.26| 2.08| 3.32| 1.2  | 0.6  | H | H | 1  |
| 110 | Cortisone          | 1 | 0.41| 1.9 | 1.63| 1.3  | 0.4  | H | H | 1  |
| 111 | Cyclizine          | 1 | 0  | 1.21| 1.55| 3.8  | 50   | H | H | 1  |
|   | Drug Name               |   |   |   |   |   |   |   |   |
|---|------------------------|---|---|---|---|---|---|---|---|
| 112| Cycloserine            | 3 | 0.48| 1.46| 1.42| -1.19| 250 | H  | L  |
| 113| Cyclosporine           | 2 | 1.17| 7.39| 9.65| 14.36| 100 | L  | H  |
| 114| Cyproheptadine         | 1 | 0   | 0.83| 1.85| 5.3  | 10  | L  | H  |
| 115| Dabigatran Etxilate    | 1 | 0.34| 3.07| 4.1  | 4.13 | 110 | L  | H  |
| 116| Dalfampridine          | 3 | 0.23| 0.71| 1.21| 0.32 | 10  | H  | H  |
| 117| Danazol                | 2 | 0.4 | 1.03| 2.58| 3.93 | 5   | H  | L  |
| 118| Dantrolene             | 1 | 0.24| 1.44| 2.5  | 1.63 | 100 | L  | H  |
| 119| Darifenacin            | 1 | 0.49| 1.58| 2.18| 3.62 | 1.6 | H  | L  |
| 120| Darunavir              | 2 | 0.64| 2.86| 3.74| 2.89 | 600 | L  | H  |
| 121| Dasatinib              | 2 | 0.76| 2.5 | 3.47| 2.88 | 70  | L  | H  |
| 122| Debrisoquine           | 1 | 0.34| 1.16| 1.37| 0.9  | 100 | H  | H  |
| 123| Delavirdine            | 2 | 0.81| 2.45| 3.89| 2.41 | 200 | L  | H  |
| 124| Demeclocycline         | 3 | 2.27| 3.57| 3.93| -0.59| 300 | H  | L  |
| 125| Desipramine            | 1 | 0.13| 0.9 | 1.58| 4.47 | 200 | L  | H  |
| 126| Desloratadine          | 2 | 0.13| 0.99| 1.55| 3.83 | 5   | H  | H  |
| 127| Desmethyldiazepam      | 1 | 0.47| 0.99| 1   | 3.02 | 5   | H  | H  |
| 128| Desogestrel            | 1 | 0.4 | 0.84| 1.96| 4.68 | 5   | H  | H  |
| 129| Dexamethasone          | 1 | 0.8 | 1.97| 2.95| 1.79 | 5   | H  | H  |
| 130| Dexamethylenidate      | 1 | 0.13| 0.94| 1.29| 2.56 | 10  | H  | L  |
| 131| Diazepam               | 1 | 0   | 1.04| 1.72| 2.96 | 10  | H  | H  |
| 132| Diazoxide              | 2 | 0.19| 0.99| 3.26| 1.42 | 5   | H  | H  |
| 133| Diclofenac             | 1 | 0.7 | 0.67| 1.95| 4.73 | 50  | L  | H  |
| 134| Dicloxacillin          | 3 | 0.84| 2.26| 1.56| 2.98 | 750 | H  | H  |
| 135| Dicoumarol             | 2 | 0.63| 1.57| 2.48| 3.66 | 100 | L  | H  |
| 136| Didanosine             | 3 | 0.31| 1.77| 1.85| -1.62| 25  | H  | L  |
| 137| Dilfurisal             | 2 | 0.7 | 0.44| 1   | 4.4  | 500 | L  | H  |
| 138| Digitoxin              | 3 | 1.27| 4.02| 4.2 | 2.85 | 0.1 | H  | L  |
| 139| Digoxin                | 3 | 1.58| 4.32| 1.82| 1.42 | 100 | H  | L  |
| 140| Dihydroquinidine       | 1 | 0.23| 1.76| 1.52| 3.27 | 40  | H  | H  |
| 141| Dilevalol              | 1 | 1   | 1.72| 2.3 | 2.5  | 50  | H  | H  |
| 142| Diloxyamide furoate    | 2 | 0.09| 1.16| 2.34| 3.09 | 500 | L  | H  |
| 143| Diltiazem              | 1 | 0   | 2.22| 2.14| 3.65 | 120 | H  | H  |
| 144| Diphenhydramine        | 1 | 0   | 0.95| 1.43| 3.45 | 50  | H  | H  |
| 145| Dipyridamole           | 2 | 0.95| 3.03| 1.22| 1.49 | 100 | H  | H  |
| 146| Disopyramide           | 3 | 0.49| 1.64| 2.26| 2.58 | 150 | H  | H  |
| 147| Disulfiram             | 2 | 0   | 1.16| 1.62| 3.88 | 250 | H  | H  |
| 148| Dofetilide             | 3 | 0.72| 2.16| 3.3 | 1.99 | 0.5 | H  | H  |
| 149| Dolasetron             | 1 | 0.31| 1.52| 1.76| 2.34 | 30  | H  | H  |
| 150| Donepezil              | 2 | 0   | 1.5 | 2.17| 4.6  | 125 | H  | H  |
|     | Name          | C0 | C1 | C2 | C3 | C4 | C5 | C6 | C7 | C8 | C9 |
|-----|---------------|----|----|----|----|----|----|----|----|----|----|
| 151 | Dosulepin     | 1  | 0  | 0.89 | 1.46 | 4.53 | 75 | L  | H  | 2  |
| 152 | Doxazosin     | 1  | 0.23 | 2.6 | 4.45 | 3.53 | 8  | H  | H  | 1  |
| 153 | Doxepin       | 1  | 0  | 0.98 | 1.46 | 4.09 | 100 | H  | H  | 1  |
| 154 | Doxyecline    | 3  | 2.1 | 3.47 | 3.88 | -0.51 | 40  | H  | L  | 3  |
| 155 | Dronabinol    | 2  | 0.5 | 0.71 | 1.04 | 7.24 | 10  | L  | H  | 2  |
| 156 | Dronedarone   | 2  | 0.36 | 1.97 | 2.98 | 8.57 | 400  | L  | H  | 2  |
| 157 | Drospernone   | 2  | 0  | 1.24 | 3.29 | 2.84 | 3  | H  | H  | 1  |
| 158 | Efavirenz     | 2  | 0.42 | 0.61 | 1.13 | 4.67 | 50  | H  | H  | 1  |
| 159 | Emtricitabine  | 3  | 0.44 | 2  | 1.86 | -1.29 | 200  | H  | L  | 3  |
| 160 | Enalapril     | 1  | 0.71 | 1.92 | 2.61 | 0.67 | 20  | H  | H  | 1  |
| 161 | Enalaprilat   | 3  | 1.28 | 1.91 | 2.08 | 0.88 | 250  | L  | L  | 3  |
| 162 | Enoxacin      | 4  | 0.73 | 1.96 | 2.45 | -1.6 | 400  | H  | L  | 3  |
| 163 | Entacapone    | 2  | 0.58 | 1.38 | 2.85 | 1.76 | 200  | L  | H  | 2  |
| 164 | Eplerenone    | 2  | 0  | 1.75 | 3.73 | 0.29 | 50  | L  | H  | 2  |
| 165 | Ergonovine    | 1  | 0.81 | 1.89 | 2.47 | 1.23 | 0.2  | H  | H  | 1  |
| 166 | Erythromycin  | 3  | 1.05 | 4.63 | 3.04 | 1.61 | 500  | H  | L  | 3  |
| 167 | Estazolam     | 2  | 0  | 0.84 | 2.01 | 2.29 | 2  | H  | H  | 1  |
| 168 | Estradiol     | 1  | 0.81 | 0.95 | 2.3  | 3.78 | 2  | H  | H  | 1  |
| 169 | Eszopiclone   | 1  | 0  | 2.43 | 3.2  | 1.25 | 3  | H  | H  | 1  |
| 170 | Ethambutol    | 3  | 0.78 | 1.72 | 0.98 | 0.12 | 400  | H  | L  | 3  |
| 171 | Ethchlorvynol | 2  | 0.4 | 0.47 | 0.82 | 1.57 | 750  | H  | H  | 1  |
| 172 | Ethinylestradiol | 1  | 0.9 | 1.02 | 3.79 | 3.86 | 0.25 | H  | L  | 3  |
| 173 | Ethosuximide  | 1  | 0.34 | 0.93 | 0.94 | 0.4  | 250  | H  | H  | 1  |
| 174 | Etidronic Acid | 3  | 1.56 | 2.54 | 1.55 | -2.54 | 400  | H  | L  | 3  |
| 175 | Etofusin      | 2  | 0.88 | 0.9  | 2.12 | 3.43 | 10  | L  | H  | 2  |
| 176 | Etoricoxib    | 2  | 0  | 1.41 | 2.77 | 2.35 | 120  | L  | H  | 2  |
| 177 | Etravirine    | 2  | 0.47 | 1.42 | 3.44 | 5.22 | 100  | L  | H  | 2  |
| 178 | Everolimus    | 1  | 0.63 | 4.73 | 4.73 | 7.1  | 1  | H  | H  | 1  |
| 179 | Exemestane    | 2  | 0  | 1.14 | 2.6  | 3.28 | 25  | L  | H  | 2  |
| 180 | Famciclovir   | 1  | 0.23 | 1.64 | 1.76 | 0.09 | 50  | H  | H  | 1  |
| 181 | Felbamate     | 4  | 0.89 | 1.19 | 2.12 | 0.5  | 600  | H  | L  | 3  |
| 182 | Felodipine    | 2  | 0.13 | 1.42 | 1.83 | 5.3  | 200  | L  | H  | 2  |
| 183 | Fenofibrate   | 2  | 0  | 1.13 | 2.11 | 5.23 | 145  | L  | H  | 2  |
| 184 | Fentanyl      | 1  | 0  | 1.33 | 2.82 | 3.62 | 15  | L  | H  | 2  |
| 185 | Fesoterodine  | 1  | 0.31 | 1.58 | 1.75 | 4.36 | 8  | H  | H  | 1  |
| 186 | Finasteride   | 1  | 0.51 | 1.6  | 3.23 | 3.01 | 5  | H  | H  | 1  |
| 187 | Flecaïnide    | 3  | 0.41 | 1.32 | 1.68 | 3.66 | 150  | H  | H  | 1  |
| 188 | Fleroxacin    | 4  | 0.57 | 1.81 | 2.37 | -0.33 | 800  | H  | L  | 3  |
| 189 | Fluconazole   | 3  | 0.31 | 1.42 | 2.45 | -0.78 | 100  | H  | H  | 1  |
|     | Drug Name     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|---------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 190 | Flucytosine   | 3   | 0.47| 1.2 | 1.27| -1.64| 500 | H   | L   | 3   |
| 191 | Flufenamic acid| 2   | 0.72| 0.59| 1.36| 5.53 | 100 | L   | H   | 2   |
| 192 | Flunarizine   | 2   | 0   | 1.37| 2.06| 6.34 | 10  | L   | H   | 2   |
| 193 | Flunitrazepam | 1   | 0   | 1.15| 2.15| 1.78 | 1   | H   | H   | 1   |
| 194 | Fluvanviteine | 1   | 0.13| 0.78| 1.19| 4.57 | 20  | H   | H   | 1   |
| 195 | Flurazepam    | 1   | 0   | 1.55| 1.89| 4.22 | 30  | H   | H   | 1   |
| 196 | Flurbiprofen  | 2   | 0.57| 0.58| 1.51| 3.75 | 100 | L   | H   | 2   |
| 197 | Flutamide     | 2   | 0.53| 0.68| 1.76| 3.34 | 125 | L   | H   | 2   |
| 198 | Fluvoxamine   | 1   | 0.23| 1.14| 0.95| 3.32 | 100 | H   | H   | 1   |
| 199 | Folic Acid    | 2   | 1.95| 3.14| 3.74| -2.31| 5   | H   | L   | 3   |
| 200 | Fosfluconazole| 1   | 0.63| 2.32| 2.99| -0.78| 100 | H   | L   | 3   |
| 201 | Fosinopril    | 2   | 0.57| 2.3 | 2.74| 7.45 | 40  | L   | H   | 2   |
| 202 | Frovatriptan  | 1   | 0.93| 1.33| 2.1 | 0.72 | 2.5 | H   | L   | 3   |
| 203 | Furosemide    | 4   | 1.25| 1.5 | 2.37| 1.9  | 80  | L   | L   | 4   |
| 204 | Gabapentin    | 3   | 0.78| 0.93| 0.99| -0.66| 800 | H   | L   | 3   |
| 205 | Galantamine   | 1   | 0.31| 1.45| 2.02| 1.03 | 5   | H   | H   | 1   |
| 206 | Gefitinib     | 2   | 0.25| 1.87| 2.97| 5.6  | 250 | L   | H   | 2   |
| 207 | Gemfibrozil    | 2   | 0.57| 0.71| 1.07| 3.94 | 600 | H   | H   | 1   |
| 208 | Glibornuride  | 1   | 0.84| 1.64| 2.46| 3.7  | 25  | L   | H   | 2   |
| 209 | Gliclazide    | 2   | 0.59| 1.66| 2.54| 1.09 | 80  | H   | H   | 1   |
| 210 | Glimepiride   | 2   | 0.75| 2.15| 3.5 | 3.96 | 4   | H   | H   | 1   |
| 211 | Glipizide     | 2   | 0.85| 2.19| 1   | 2.57 | 250 | H   | H   | 1   |
| 212 | Glyburide     | 2   | 0.85| 2.01| 1.77| 4.24 | 40  | L   | H   | 2   |
| 213 | Granisetron   | 1   | 0.26| 1.56| 2.38| 1.72 | 1   | H   | H   | 1   |
| 214 | Griseofulvin  | 2   | 0   | 1.58| 1.87| 1.91 | 100 | H   | H   | 1   |
| 215 | Guanabenz     | 1   | 0.48| 1.2 | 1.02| 2.98 | 16  | H   | H   | 1   |
| 216 | Haloperidol   | 2   | 0.31| 1.45| 2.08| 3.85 | 20  | L   | H   | 2   |
| 217 | Hexobarbital  | 1   | 0.24| 1.33| 1.5 | 1.63 | 250 | H   | H   | 1   |
| 218 | Hydrochlorothiazide| 3 | 1.01| 1.76| 2.77| -0.37| 50  | H   | L   | 3   |
| 219 | Hydrocodone   | 1   | 0   | 1.42| 2.12| 1.13 | 10  | H   | H   | 1   |
| 220 | Hydroflumethiazide| 3 | 1.01| 1.72| 2.44| -0.21| 50  | H   | L   | 3   |
| 221 | Hydromorphone | 1   | 0.27| 1.32| 1.79| 0.72 | 8   | H   | H   | 1   |
| 222 | Hydroxychloroquine| 1 | 0.36| 1.66| 1.84| 4.12 | 200 | H   | H   | 1   |
| 223 | Hydroxyurea   | 3   | 0.91| 0.98| 1.4 | -1.8 | 1000| H   | L   | 3   |
| 224 | Hydroxyzine   | 1   | 0.23| 1.8 | 2.41| 4   | 30  | L   | H   | 2   |
| 225 | Hyoscyamine   | 3   | 0.31| 1.31| 1.63| 1.3  | 311 | H   | H   | 1   |
| 226 | Ibandronate   | 3   | 1.56| 3.05| 1.76| -3.37| 150 | H   | L   | 3   |
| 227 | Ibuprofen     | 2   | 0.57| 0.51| 1.01| 3.68 | 800 | H   | H   | 1   |
| 228 | Iloperidone   | 2   | 0   | 1.73| 2.85| 4.27 | 12  | L   | H   | 2   |
|    | Name                      | M     | F     | C     | R     | L     | H     | 1    |
|---|---------------------------|-------|-------|-------|-------|-------|-------|------|
| 229| Imidapril                 | 0.71  | 2.22  | 2.85  | 1.53  | 10    | H     | H    |
| 230| Imipramine               | 0     | 0.95  | 1.59  | 5.04  | 50    | L     | H    |
| 231| Indobufen                | 0.57  | 1.15  | 1.66  | 3.27  | 300   | H     | 1    |
| 232| Indomethacin             | 0.57  | 1.24  | 2.49  | 4.18  | 50    | L     | H    |
| 233| Irbesartan               | 0.63  | 1.69  | 2.71  | 6.04  | 300   | L     | H    |
| 234| Isoniazid                | 0.47  | 1.39  | 1.85  | -0.67 | 300   | H     | L    |
| 235| Isosorbide Dinitrate     | 0     | 0.79  | 1.75  | 0.22  | 40    | H     | H    |
| 236| Isotretinoin             | 0.57  | 0.8   | 0.98  | 6.74  | 10    | L     | H    |
| 237| Itraconazole             | 0     | 2.95  | 4.54  | 5.99  | 100   | L     | H    |
| 238| Ivabradine               | 1     | 0     | 2.35  | 3.25  | 3.97  | 7.5   | H    |
| 239| Ketanserin               | 0.26  | 1.82  | 2.01  | 3     | 25    | L     | H    |
| 240| Ketoconazole             | 0     | 2.22  | 3.76  | 3.64  | 200   | L     | H    |
| 241| Ketorolac                | 0.57  | 0.98  | 2.06  | 1.62  | 10    | L     | H    |
| 242| Labetalol                | 1     | 1     | 1.72  | 2.15  | 2.5   | 200   | L     |
| 243| Lacosamide               | 0.53  | 1.48  | 2.55  | 0.39  | 50    | H     | H    |
| 244| Lamivudine               | 0.44  | 2.02  | 1.92  | -1.46 | 300   | H     | L    |
| 245| Lamotrigine              | 0.45  | 0.93  | 2.13  | 2.53  | 200   | L     | H    |
| 246| Lansoprazole             | 0.35  | 1.73  | 2.97  | 2.6   | 30    | L     | H    |
| 247| Lapatinib ditosylate     | 0.33  | 2.13  | 3.87  | 5.97  | 250   | L     | H    |
| 248| Leflunomide              | 0.47  | 0.81  | 2.17  | 2.32  | 10    | L     | H    |
| 249| Lenalidomide             | 0.56  | 1.91  | 2.53  | 0.53  | 200   | H     | H    |
| 250| Letrozole                | 0     | 0.97  | 2.92  | 1.24  | 2.5   | 2    |
| 251| Leucovorin               | 3     | 2.16  | 4.11  | 4.65  | -3.49 | 25    | H    |
| 252| Levamisole               | 0     | 0.88  | 1.01  | 1.84  | 50    | H     | H    |
| 253| Levetiracetam            | 0.49  | 1.32  | 1.87  | -0.34 | 1000  | H     | L    |
| 254| Levocetirizine           | 0.57  | 1.76  | 2.24  | 2.08  | 10    | H     | H    |
| 255| Levodopa                 | 1.56  | 1.44  | 1.77  | -2.82 | 250   | H     | L    |
| 256| Levonorgestrel           | 0.4   | 1.07  | 2.45  | 3.31  | 0.75  | H     | H    |
| 257| Linezolid                | 0.27  | 1.72  | 1.35  | 1.17  | 1.5   | H     | H    |
| 258| Loperamide               | 0.31  | 1.88  | 2.9   | 4.66  | 2     | H     | H    |
| 259| Lopinavir                | 0.92  | 2.89  | 4.57  | 6.1   | 200   | L     | H    |
| 260| Loracarbef               | 1.06  | 2.42  | 3.26  | -0.47 | 400   | H     | L    |
| 261| Loratadine               | 0     | 1.14  | 2.17  | 5.05  | 10    | L     | H    |
| 262| Lorazepam                | 0.64  | 1.29  | 1.83  | 2.37  | 2     | H     | H    |
| 263| Lovastatin               | 0.31  | 1.44  | 2.34  | 4.08  | 40    | L     | H    |
| 264| Maprotiline              | 0.13  | 0.68  | 1.27  | 4.52  | 75    | H     | H    |
| 265| Mebendazole              | 0.71  | 1.38  | 2.76  | 3.08  | 100   | L     | H    |
| 266| Mefenamic acid           | 0.65  | 0.7   | 1.47  | 5.29  | 250   | L     | H    |
| 267| Mefloquine               | 0.38  | 1.22  | 1.04  | 3.67  | 250   | H     | H    |
| Compound                  | Value 1 | Value 2 | Value 3 | Value 4 | Value 5 | Value 6 | Value 7 | Value 8 | Value 9 | Value 10 | Value 11 | Value 12 | Value 13 | Value 14 | Value 15 | Value 16 | Value 17 |
|---------------------------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|
| Melatonin                 | 0.57    | 1.11    | 1.92    | 1.03    | 12      | H       | H       | 1       |
| Meloxicam                 | 0.72    | 2.02    | 3.12    | 2.29    | 15      | L       | H       | 2       |
| Melphalan                 | 0.78    | 1.37    | 1.9     | -0.21   | 2       | H       | L       | 3       |
| Meperidine                | 1       | 0.97    | 3.13    | 2.23    | 20      | H       | H       | 1       |
| Meprobamate               | 0.89    | 1.12    | 1.62    | 0.92    | 400     | H       | L       | 3       |
| Mercaptopurine            | 0.43    | 0.7     | 1.31    | 0.82    | 50      | H       | H       | 1       |
| Mesalamine                | 0.93    | 0.7     | 1.52    | 1.06    | 1200    | H       | L       | 3       |
| Metaxalone                | 0.23    | 0.86    | 1.47    | 2.15    | 800     | H       | H       | 1       |
| Metformin                 | 0.55    | 1.68    | 0.58    | -1.63   | 1000    | H       | L       | 3       |
| Methazolamide             | 0.44    | 2.01    | 2.5     | 0.09    | 500     | H       | H       | 1       |
| Methotrexate              | 3       | 1.85    | 2.82    | 4.23    | -0.53   | 15      | L       | 4       |
| Methyldopa                | 3       | 1.56    | 1.45    | 1.73    | -2.26   | 500     | H       | L       | 3       |
| Methylergonovine          | 0.81    | 1.89    | 2.47    | 1.76    | 0.2     | H       | H       | 1       |
| Methylenephidate          | 0.13    | 0.94    | 1.29    | 2.56    | 20      | H       | H       | 1       |
| Methylprednisolone        | 0.73    | 2       | 3       | 1.74    | 32      | L       | H       | 2       |
| Metoprolol                | 0.29    | 1.52    | 2.9     | 1.49    | 75      | H       | H       | 1       |
| Metronidazole             | 0.31    | 0.86    | 1.75    | -0.46   | 500     | H       | H       | 1       |
| Mexiletine                | 0.23    | 0.9     | 3.71    | 2.57    | 10      | L       | H       | 2       |
| Mianserin                 | 1       | 0.16    | 1.03    | 1.35    | 3.76    | 50      | H       | H       | 1       |
| Miglitol                  | 3       | 1.18    | 1.23    | 1.57    | -1.26   | 100     | H       | L       | 3       |
| Miglustat                 | 3       | 0.93    | 1.95    | 1.36    | 0.91    | 100     | H       | L       | 3       |
| Milnacipran               | 3       | 0.21    | 1.33    | 2.32    | 1.91    | 500     | H       | H       | 1       |
| Minoxidil                 | 1       | 0.52    | 2.07    | 1.05    | -0.72   | 10      | H       | L       | 3       |
| Mitrazapine               | 1       | 0       | 1.52    | 2.16    | 2.81    | 45      | H       | H       | 1       |
| Mispolostil               | 1       | 0.63    | 1.43    | 1.77    | 3.07    | 0.2     | H       | H       | 1       |
| Mizolastine               | 2       | 0.39    | 2.15    | 3.09    | 2.84    | 10      | L       | H       | 2       |
| Modafinil                 | 2       | 0.49    | 1.47    | 3.2     | 0.94    | 200     | L       | H       | 2       |
| Molindone                 | 1       | 0.31    | 1.29    | 1.57    | 2.57    | 50      | H       | H       | 1       |
| Mycofenolate mofetil      | 2       | 0.13    | 1.66    | 1.96    | 2.98    | 500     | H       | H       | 1       |
| Nabumetone                | 2       | 0       | 0.7     | 3.34    | 2.98    | 500     | L       | H       | 2       |
| Nadolol                   | 3       | 0.83    | 1.9     | 1.56    | 0.38    | 160     | H       | L       | 3       |
| Nalidixic acid            | 2       | 0.57    | 1.34    | 1.1     | 1.02    | 1200    | H       | H       | 1       |
| Naproxen                  | 2       | 0.57    | 0.75    | 1.49    | 2.82    | 500     | H       | H       | 1       |
| Naratriptan               | 3       | 0.68    | 1.62    | 2.14    | 1.7     | 2.5     | H       | H       | 1       |
| Nateglinide               | 2       | 0.83    | 1.12    | 2.02    | 4.3     | 120     | L       | H       | 2       |
| Nefazodone                | 2       | 1       | 2.12    | 2.8     | 5.73    | 100     | L       | H       | 2       |
| Nefopam                   | 1       | 0       | 0.92    | 1.46    | 2.91    | 30      | H       | H       | 1       |
| Nelfinavir                | 2       | 1.27    | 2.81    | 3.72    | 5.84    | 200     | L       | H       | 2       |
| Neostigmine               | 3       | 0       | 0.73    | 1.21    | -2.81   | 15      | H       | L       | 3       |
|   |   | 0.57 | 0.13 | 0.29 | 0.39 | 0.38 | 0 | 0.26 | 0.72 | 0.13 | 0.74 | 0.43 | 0.13 | 0.47 | 0.13 | 0.27 | 0.71 | 0.4 | 0.2 | 0.13 | 3.55 | 0.57 | 0.13 | 0.95 | 1 | 0 | 0.26 | 0.57 | 0.38 | 0.39 | 0.29 | 0.23 | 0.5 | 0.31 | 0.13 | 0.57 | 0.78 |
|---|---|-----|------|------|------|------|---|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|   | Drug               |   |   |   |   |   |   |   |   |   |   |   |   |
|---|--------------------|---|---|---|---|---|---|---|---|---|---|---|---|
| 346| Penicillin V       | 4 | 0.84| 2.27| 2.86| 1.94| 500| H  | H  | H  |1  |
| 347| Pentazocine        | 2 | 0.5 | 1.04| 1.38| 4.67| 600| L  | H  | H  |2  |
| 348| Pentoxyfiline      | 1 | 0  | 1.59| 2.42| 0.12| 400| H  | H  |1  |
| 349| Perhexiline        | 2 | 0.13| 0.56| 0.62| 7.15| 100| H  | H  |1  |
| 350| Perindopril erbumine | 1 | 0.71| 1.88| 2.23| 1.21| 8  | H  | H  |1  |
| 351| Phencetin          | 2 | 0.41| 0.87| 1.55| 1.71| 500| H  | H  |1  |
| 352| Phenobarbital      | 1 | 0.52| 1.29| 1.81| 1.37| 60 | H  | H  |1  |
| 353| Phenylbutazone     | 1 | 0  | 1.63| 2.45| 3.39| 100| L  | H  |2  |
| 354| Phenylethylmalonamide | 3 | 0.97| 1.25| 2.41| 0.01| 250| H  | L  |3  |
| 355| Pimozide           | 1 | 0.33| 1.44| 2.6 | 6.4 | 2  | H  | H  |1  |
| 356| Pindolol           | 3 | 0.6 | 1.51| 1.38| 1.67| 50 | H  | H  |1  |
| 357| Pioglitazone       | 2 | 0.34| 1.64| 2.44| 3.53| 100| L  | H  |2  |
| 358| Piperazine         | 3 | 0.29| 0.89| 0.63| -1.48| 500| H  | L  |3  |
| 359| Piracetam          | 3 | 0.49| 1.28| 1.88| -1.18| 800| H  | L  |3  |
| 360| Pirenzepine        | 3 | 0.42| 2.42| 3.13| -0.35| 50 | H  | H  |1  |
| 361| Piroxicam          | 2 | 0.72| 2.12| 3.12| 1.89| 20 | L  | H  |2  |
| 362| Pramipexole        | 3 | 0.36| 0.97| 2.69| 1.17| 600| L  | H  |2  |
| 363| Prasugrel          | 2 | 0  | 1.3 | 1.57| 3.43| 600| H  | H  |1  |
| 364| Prazepam           | 2 | 0  | 1.05| 2.38| 3.93| 200| L  | H  |2  |
| 365| Prazosin           | 1 | 0.23| 2.17| 3.59| 2.03| 5  | H  | H  |1  |
| 366| Prednisolone       | 1 | 0.72| 2  | 4.46| 1.42| 0.25| H  | H  |1  |
| 367| Prednisone         | 2 | 0.41| 1.97| 3.25| 1.66| 50 | L  | H  |2  |
| 368| Primaxine          | 1 | 0.34| 1.49| 1.76| 2.6 | 15 | H  | H  |1  |
| 369| Primidone          | 2 | 0.51| 1.45| 2.65| 0.88| 8  | H  | H  |1  |
| 370| Probenecid         | 2 | 0.57| 1.29| 2.65| 3.37| 2  | H  | H  |1  |
| 371| Probucol           | 2 | 0.62| 1.2 | 1.38| 10.97| 500| L  | H  |2  |
| 372| Procainamide       | 3 | 0.5 | 1.49| 2.11| 1.42| 1000| H  | H  |1  |
| 373| Prochlorperazine   | 1 | 0  | 1.47| 2.11| 4.38| 10 | L  | H  |2  |
| 374| Progesterone       | 2 | 0  | 1.04| 2.49| 3.78| 200| L  | H  |2  |
| 375| Proguanil          | 1 | 0.74| 1.59| 1.19| 2.53| 100| H  | H  |1  |
| 376| Promazine          | 1 | 0  | 1.06| 1.72| 4.4 | 50 | L  | H  |2  |
| 377| Promethazine       | 1 | 0  | 1.09| 1.74| 4.4 | 100| L  | H  |2  |
| 378| Propylthiouracil   | 1 | 0.39| 1.03| 1.74| 0.97| 50 | H  | H  |1  |
| 379| Protriptyline      | 1 | 0.13| 0.73| 1.34| 4.87| 10 | L  | H  |2  |
| 380| Pseudoephedrine    | 3 | 0.38| 1.12| 0.94| 0.89| 120| H  | H  |1  |
| 381| Pyrazinamide       | 1 | 0.49| 1.04| 1.68| -0.68| 500| H  | L  |3  |
| 382| Pyridostigmine     | 3 | 0  | 0.7 | 1.23| -4.26| 60 | H  | L  |3  |
| 383| Pyrimethamine      | 3 | 0.45| 0.99| 2.69| 3  | 40 | L  | H  |2  |
| 384| Quinacrine         | 1 | 0.13| 1.56| 2.05| 6.72| 100| L  | H  |2  |
| N  | Drug Name          | Type | Value 1 | Value 2 | Value 3 | Value 4 | Value 5 | Value 6 | Value 7 | Value 8 | Value 9 | Value 10 | Value 11 | Value 12 | Value 13 | Value 14 | Value 15 | Value 16 | Value 17 | Value 18 | Value 19 | Value 20 | Value 21 | Value 22 | Value 23 | Value 24 | Value 25 | Value 26 | Value 27 | Value 28 | Value 29 | Value 30 | Value 31 | Value 32 | Value 33 | Value 34 | Value 35 | Value 36 | Value 37 | Value 38 | Value 39 | Value 40 | Value 41 | Value 42 | Value 43 | Value 44 | Value 45 | Value 46 | Value 47 | Value 48 | Value 49 | Value 50 | Value 51 | Value 52 | Value 53 | Value 54 | Value 55 | Value 56 | Value 57 | Value 58 | Value 59 | Value 60 | Value 61 | Value 62 | Value 63 | Value 64 | Value 65 | Value 66 | Value 67 | Value 68 | Value 69 | Value 70 | Value 71 | Value 72 | Value 73 | Value 74 | Value 75 | Value 76 | Value 77 | Value 78 | Value 79 | Value 80 | Value 81 | Value 82 | Value 83 | Value 84 | Value 85 | Value 86 | Value 87 | Value 88 | Value 89 | Value 90 | Value 91 | Value 92 | Value 93 | Value 94 | Value 95 | Value 96 | Value 97 | Value 98 | Value 99 | Value 100 | Value 101 | Value 102 | Value 103 | Value 104 | Value 105 | Value 106 | Value 107 | Value 108 | Value 109 | Value 110 | Value 111 | Value 112 | Value 113 | Value 114 | Value 115 | Value 116 | Value 117 | Value 118 | Value 119 | Value 120 | Value 121 | Value 122 | Value 123 | Value 124 | Value 125 | Value 126 | Value 127 | Value 128 | Value 129 | Value 130 | Value 131 | Value 132 | Value 133 | Value 134 | Value 135 | Value 136 | Value 137 | Value 138 | Value 139 | Value 140 | Value 141 | Value 142 | Value 143 | Value 144 | Value 145 | Value 146 | Value 147 | Value 148 | Value 149 | Value 150 | Value 151 | Value 152 | Value 153 | Value 154 | Value 155 | Value 156 | Value 157 | Value 158 | Value 159 | Value 160 | Value 161 | Value 162 | Value 163 | Value 164 | Value 165 | Value 166 | Value 167 | Value 168 | Value 169 | Value 170 | Value 171 | Value 172 | Value 173 | Value 174 | Value 175 | Value 176 | Value 177 | Value 178 | Value 179 | Value 180 | Value 181 | Value 182 | Value 183 | Value 184 | Value 185 | Value 186 | Value 187 | Value 188 | Value 189 | Value 190 | Value 191 | Value 192 | Value 193 | Value 194 | Value 195 | Value 196 | Value 197 | Value 198 | Value 199 | Value 200 | Value 201 | Value 202 | Value 203 | Value 204 | Value 205 | Value 206 | Value 207 | Value 208 | Value 209 | Value 210 | Value 211 | Value 212 | Value 213 | Value 214 | Value 215 | Value 216 | Value 217 | Value 218 | Value 219 | Value 220 | Value 221 | Value 222 | Value 223 | Value 224 | Value 225 | Value 226 | Value 227 | Value 228 | Value 229 | Value 230 | Value 231 | Value 232 | Value 233 | Value 234 | Value 235 | Value 236 | Value 237 | Value 238 | Value 239 | Value 240 | Value 241 | Value 242 | Value 243 | Value 244 | Value 245 | Value 246 | Value 247 | Value 248 | Value 249 | Value 250 | Value 251 | Value 252 | Value 253 | Value 254 | Value 255 | Value 256 | Value 257 | Value 258 | Value 259 | Value 260 | Value 261 | Value 262 | Value 263 | Value 264 | Value 265 | Value 266 | Value 267 | Value 268 | Value 269 | Value 270 | Value 271 | Value 272 | Value 273 | Value 274 | Value 275 | Value 276 | Value 277 | Value 278 | Value 279 | Value 280 | Value 281 | Value 282 | Value 283 | Value 284 | Value 285 | Value 286 | Value 287 | Value 288 | Value 289 | Value 290 | Value 291 | Value 292 | Value 293 | Value 294 | Value 295 | Value 296 | Value 297 | Value 298 | Value 299 | Value 300 | Value 301 | Value 302 | Value 303 | Value 304 | Value 305 | Value 306 | Value 307 | Value 308 | Value 309 | Value 310 | Value 311 | Value 312 | Value 313 | Value 314 | Value 315 | Value 316 | Value 317 | Value 318 | Value 319 | Value 320 | Value 321 | Value 322 | Value 323 | Value 324 | Value 325 | Value 326 | Value 327 | Value 328 | Value 329 | Value 330 | Value 331 | Value 332 | Value 333 | Value 334 | Value 335 | Value 336 | Value 337 | Value 338 | Value 339 | Value 340 | Value 341 | Value 342 | Value 343 | Value 344 | Value 345 | Value 346 | Value 347 | Value 348 | Value 349 | Value 350 | Value 351 | Value 352 | Value 353 | Value 354 | Value 355 | Value 356 | Value 357 | Value 358 | Value 359 | Value 360 | Value 361 | Value 362 | Value 363 | Value 364 | Value 365 | Value 366 | Value 367 | Value 368 | Value 369 | Value 370 | Value 371 | Value 372 | Value 373 | Value 374 | Value 375 | Value 376 | Value 377 | Value 378 | Value 379 | Value 380 | Value 381 | Value 382 | Value 383 | Value 384 | Value 385 | Value 386 | Value 387 | Value 388 | Value 389 | Value 390 | Value 391 | Value 392 | Value 393 | Value 394 | Value 395 | Value 396 | Value 397 | Value 398 | Value 399 | Value 400 | Value 401 | Value 402 | Value 403 | Value 404 | Value 405 | Value 406 | Value 407 | Value 408 | Value 409 | Value 410 | Value 411 | Value 412 | Value 413 | Value 414 | Value 415 | Value 416 | Value 417 | Value 418 | Value 419 | Value 420 | Value 421 | Value 422 | Value 423 |
|   |   |   |   |   |   |
|---|---|---|---|---|---|
| 424 | Sulindac | 2 | 0.57 | 1.39 | 2.72 | 3.16 | 200 | L | H | 2 |
| 425 | Sulpiride | 3 | 0.72 | 2.15 | 1.78 | 1.11 | 200 | H | H | 1 |
| 426 | Tacrine | 1 | 0.23 | 0.76 | 2.3 | 3.27 | 200 | L | L | 2 |
| 427 | Tacrolimus | 2 | 0.71 | 3.98 | 3.98 | 5.78 | 5 | H | H | 1 |
| 428 | Tadalafil | 2 | 0.31 | 2.27 | 3.27 | 2.58 | 20 | L | H | 2 |
| 429 | Talinolol | 3 | 0.81 | 2 | 1.97 | 3.15 | 100 | H | H | 1 |
| 430 | Tamoxifen | 1 | 0 | 1.11 | 1.85 | 6.82 | 20 | L | H | 2 |
| 431 | Tamsulosin | 1 | 0.59 | 2.11 | 2.9 | 2.17 | 0.4 | H | H | 1 |
| 432 | Telmisartan | 2 | 0.57 | 1.59 | 3.56 | 7.54 | 80 | L | H | 2 |
| 433 | Temazepam | 1 | 0.17 | 1.34 | 2.35 | 2.34 | 100 | L | H | 2 |
| 434 | Temozolomide | 2 | 0.49 | 1.82 | 2.49 | -0.81 | 250 | H | L | 3 |
| 435 | Tenofovir disoproxil | 3 | 0.23 | 3.22 | 1.21 | 0.8 | 100 | H | H | 1 |
| 436 | Tenoxicam | 1 | 0.72 | 2.06 | 3.04 | 1.61 | 20 | L | H | 2 |
| 437 | Terbinafine | 2 | 0 | 0.86 | 1.34 | 5.96 | 250 | L | H | 2 |
| 438 | Terbutaline | 3 | 1.38 | 1.63 | 1.31 | 0.48 | 5 | H | L | 3 |
| 439 | Terfenadine | 2 | 0.63 | 1.8 | 2.04 | 6.07 | 60 | L | H | 2 |
| 440 | Testolactone | 2 | 0 | 1.03 | 2.17 | 2.63 | 50 | L | H | 2 |
| 441 | Testosterone | 2 | 0.31 | 1.01 | 2.27 | 3.22 | 40 | L | H | 2 |
| 442 | Tetrabenazine | 2 | 0 | 1.44 | 2.02 | 3.81 | 25 | L | H | 2 |
| 443 | Thalidomide | 2 | 0.34 | 1.72 | 2.74 | 0.53 | 25 | H | H | 1 |
| 444 | Theophylline | 1 | 0.35 | 1.29 | 1.99 | -0.03 | 600 | H | H | 1 |
| 445 | Thioguanine | 1 | 0.77 | 1.14 | 1.47 | -1.7 | 40 | H | L | 3 |
| 446 | Thioridazine | 1 | 0 | 1.13 | 1.93 | 6 | 200 | L | H | 2 |
| 447 | Thyroxine | 2 | 1.03 | 1.31 | 2.83 | 3.51 | 0.3 | H | H | 1 |
| 448 | Tiaprofenic acid | 2 | 0.57 | 0.81 | 1.89 | 2.54 | 300 | L | H | 2 |
| 449 | Ticlopidine | 1 | 0 | 0.62 | 1.32 | 4.39 | 250 | L | H | 2 |
| 450 | Tilidine | 1 | 0 | 1.07 | 1.61 | 3.76 | 60 | H | H | 2 |
| 451 | Tiludronic acid | 3 | 1.25 | 2.46 | 2.06 | 0.26 | 200 | H | L | 3 |
| 452 | Tinidazole | 1 | 0 | 1.13 | 2.4 | -0.32 | 500 | H | H | 1 |
| 453 | Tizanidine | 2 | 0.39 | 1.19 | 1.69 | 2.09 | 80 | H | H | 1 |
| 454 | Tocainide | 3 | 0.47 | 1.24 | 1.62 | 0.26 | 600 | H | H | 1 |
| 455 | Tolbutamide | 2 | 0.93 | 1.09 | 2.3 | 2.5 | 300 | H | H | 1 |
| 456 | Tolcapone | 2 | 0.8 | 0.89 | 2.25 | 3.25 | 200 | L | H | 2 |
| 457 | Toltenamic acid | 2 | 0.71 | 0.69 | 1.64 | 5.66 | 200 | L | H | 2 |
| 458 | Tolmetin | 2 | 0.57 | 0.97 | 1.93 | 2.21 | 600 | H | H | 2 |
| 459 | Tolterodine | 1 | 0.5 | 1.08 | 1.42 | 5.24 | 2 | H | H | 1 |
| 460 | Tolvaptan | 2 | 0.72 | 1.86 | 3.31 | 4.65 | 30 | L | H | 2 |
| 461 | Topiramate | 3 | 0.44 | 2.17 | 1.77 | 0.04 | 300 | H | H | 1 |
| 462 | Topotecan | 3 | 0.67 | 2.73 | 3.69 | 0.73 | 1 | H | H | 1 |

265
|   |   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|
| 463 | Toremifene | 1 | 0 | 1.11 | 1.99 | 6.53 | 60 | L | H | 2 |
| 464 | Torsemide | 2 | 0.72 | 1.75 | 3.04 | 3.36 | 100 | L | H | 2 |
| 465 | Tramadol | 1 | 0.31 | 1.3 | 1.15 | 3.1 | 50 | H | H | 1 |
| 466 | Trandolapril | 2 | 0.71 | 1.96 | 1.47 | 2.1 | 6 | H | H | 1 |
| 467 | Tretinoin | 2 | 0.57 | 0.8 | 0.98 | 6.74 | 40 | L | H | 2 |
| 468 | Triamcinolone | 1 | 1.03 | 2.25 | 3.21 | 0.71 | 4 | H | L | 3 |
| 469 | Triamcinolone acetonide | 1 | 0.56 | 2.14 | 3.13 | 2.21 | 4 | H | H | 1 |
| 470 | Triamterene | 2 | 0.68 | 1.45 | 2.64 | 1.61 | 100 | L | H | 2 |
| 471 | Triclabendazole | 2 | 0.35 | 0.9 | 2.25 | 6.44 | 250 | L | H | 2 |
| 472 | Trifluoperazine | 1 | 0 | 1.42 | 1.79 | 4.69 | 10 | L | H | 2 |
| 473 | Trihexyphenidyl | 1 | 0.31 | 1.08 | 1.16 | 5.15 | 5 | H | H | 1 |
| 474 | Trimetazidine | 3 | 0.16 | 1.67 | 2 | 1.18 | 20 | H | H | 1 |
| 475 | Trimethoprim | 3 | 0.45 | 1.62 | 2.81 | 0.98 | 160 | L | H | 2 |
| 476 | Tropisetron | 1 | 0.31 | 1.21 | 1.78 | 2.88 | 5 | H | H | 1 |
| 477 | Trospium | 3 | 0.17 | 1.1 | 1.57 | -1.16 | 20 | H | H | 1 |
| 478 | Ursodiol | 2 | 1.2 | 1.35 | 2.4 | 4.51 | 500 | L | H | 2 |
| 479 | Valacyclovir | 1 | 0.63 | 2.75 | 2.44 | -1.22 | 1000 | H | L | 3 |
| 480 | Valdecoxib | 2 | 0.44 | 1.24 | 2.5 | 1.83 | 20 | L | H | 2 |
| 481 | Valganciclovir | 1 | 0.86 | 3.15 | 2.64 | -2.18 | 450 | H | L | 3 |
| 482 | Valproic Acid | 1 | 0.61 | 0.46 | 0.54 | 2.76 | 250 | H | L | 1 |
| 483 | Valsartan | 4 | 1.21 | 1.82 | 3.32 | 4.86 | 320 | L | H | 2 |
| 484 | Vardenafil | 1 | 0.13 | 2.97 | 1.26 | 2.23 | 100 | H | H | 1 |
| 485 | Vigabatrin | 3 | 0.78 | 0.99 | 0.99 | -2.22 | 500 | H | L | 3 |
| 486 | Vitamin A (Retinol) | 2 | 0.31 | 0.75 | 0.81 | 6.4 | 110 | H | H | 1 |
| 487 | Vitamin B1 | 3 | 0.54 | 1.04 | 1.58 | -5.97 | 500 | H | L | 3 |
| 488 | Vitamin B2 | 4 | 1.33 | 2.69 | 2.71 | -0.73 | 100 | H | L | 3 |
| 489 | Vitamin D3 | 1 | 0.31 | 0.71 | 0.75 | 9.48 | 1.4 | H | H | 1 |
| 490 | Voriconazole | 2 | 0.31 | 1.5 | 2.19 | 0.52 | 200 | H | H | 1 |
| 491 | Zafirlukast | 2 | 0.85 | 2.13 | 4.09 | 7.09 | 20 | L | H | 2 |
| 492 | Zidovudine | 1 | 0.47 | 1.7 | 2.03 | 0.04 | 200 | H | H | 1 |
| 493 | Zileuton | 2 | 0.71 | 1.15 | 2.12 | 2.48 | 600 | L | H | 2 |
| 494 | Zolmitriptan | 1 | 0.48 | 1.65 | 2.67 | 1.29 | 5 | H | H | 1 |
| 495 | Zonisamide | 1 | 0.44 | 1.11 | 1.95 | -0.36 | 100 | H | H | 1 |
| 496 | Zopiclone | 1 | 0 | 2.43 | 3.2 | 1.25 | 7.5 | H | H | 1 |

**Test set**

|   |   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Acitretin | 2 | 0.57 | 0.97 | 1.32 | 6.07 | 25 | L | H | 2 |
| 2 | Alfuzosin | 1 | 0.48 | 2.24 | 3.39 | 3.55 | 10 | L | H | 2 |
| 3 | Aliskiren | 1 | 1.2 | 3.06 | 3.65 | 3.51 | 300 | L | H | 2 |
| 4 | Aminocaproic acid | 3 | 0.78 | 0.91 | 0.95 | -2.24 | 1000 | H | L | 3 |
| 5  | Amprenavir  | 2   | 0.61 | 2.61 | 3.52 | 3.29 | 50   | L    | H    | 2    |
| 6  | Armodafinil | 2   | 0.49 | 1.47 | 3.2  | 0.94 | 250  | L    | H    | 2    |
| 7  | Aspirin     | 1   | 0.57 | 0.77 | 1.42 | 1.02 | 500  | H    | H    | 1    |
| 8  | Auranofin   | 4   | 0    | 1.82 | 2.17 | 3.79 | 3    | H    | H    | 1    |
| 9  | Azapropazone| 4   | 0    | 2.16 | 2.1  | 1.79 | 300  | H    | H    | 1    |
| 10 | Baclofen    | 3   | 0.78 | 1.02 | 1.47 | -0.62| 20   | H    | L    | 3    |
| 11 | Betaxolol   | 1   | 0.29 | 1.53 | 1.31 | 2.32 | 20   | H    | H    | 1    |
| 12 | Bevantolol  | 2   | 0.29 | 1.82 | 2.14 | 3    | 200  | H    | H    | 1    |
| 13 | Bezafibrate | 2   | 0.83 | 1.35 | 2.54 | 3.7  | 200  | L    | H    | 2    |
| 14 | Bromazepam  | 1   | 0.47 | 1.27 | 1.93 | 1.7  | 6    | H    | H    | 1    |
| 15 | Bromocriptine| 1  | 0.79 | 3.66 | 4.28 | 6.58 | 5    | H    | H    | 1    |
| 16 | Capecitabine| 1   | 0.6  | 2.4  | 2.41 | 0.84 | 500  | H    | H    | 1    |
| 17 | Carprofidine| 1   | 0    | 1.12 | 1.45 | 9.97 | 2000 | L    | H    | 2    |
| 18 | Carvedilol  | 2   | 0.62 | 2.09 | 3    | 4.04 | 25   | L    | H    | 2    |
| 19 | Cefixime    | 4   | 1.64 | 3.12 | 4.01 | 0.25 | 400  | L    | L    | 4    |
| 20 | Cefuroxim   | 2   | 0.44 | 1.22 | 2.43 | 4.37 | 200  | L    | H    | 2    |
| 21 | Cetirizine  | 3   | 0.61 | 2.35 | 2.34 | 1.86 | 200  | H    | H    | 1    |
| 22 | Cephalexin  | 3   | 1.06 | 2.54 | 3.27 | -1.84| 750  | H    | L    | 3    |
| 23 | Cevimeline  | 1   | 0    | 0.9  | 0.86 | 1.14 | 30   | H    | H    | 1    |
| 24 | Chloral hydrate| 1 | 0.75 | 0.59 | 0.97 | 0.72 | 500  | H    | H    | 1    |
| 25 | Chloramphenicol| 1 | 0.87 | 1.65 | 2.66 | 1.28 | 250  | L    | H    | 2    |
| 26 | Cinacalcet  | 2   | 0.13 | 0.63 | 1.37 | 6.35 | 90   | L    | H    | 2    |
| 27 | Ciprofloxacin| 4  | 0.73 | 1.85 | 2.5  | -0.73| 750  | H    | H    | 3    |
| 28 | Clobazam    | 1   | 0    | 1.47 | 2.49 | 2.44 | 10   | L    | H    | 2    |
| 29 | Clomipramine| 1   | 0    | 0.89 | 1.66 | 5.92 | 75   | L    | H    | 2    |
| 30 | Clonidine   | 3   | 0.39 | 0.9  | 1.19 | 1.73 | 0.3  | H    | H    | 1    |
| 31 | Clorazepate | 1   | 1.04 | 1.34 | 2.14 | 2.51 | 15   | L    | H    | 2    |
| 32 | Clotrimazole| 2   | 0    | 0.78 | 2.37 | 5.25 | 10   | L    | H    | 2    |
| 33 | Cyclobenzaprine| 1 | 0    | 0.83 | 1.41 | 5.1  | 10   | L    | H    | 2    |
| 34 | Cyclophosphamide| 1 | 0.14 | 1.18 | 2.2  | 0.8  | 50   | H    | H    | 1    |
| 35 | Dapsone     | 2   | 0.45 | 1.35 | 2.84 | 0.89 | 100  | L    | H    | 2    |
| 36 | Desmopressin| 3   | 4.3  | 8.13 | 11.82| -3.14| 0.2  | H    | L    | 3    |
| 37 | Desvenlafaxine| 3 | 0.81 | 1.22 | 1.34 | 2.68 | 100  | H    | H    | 1    |
| 38 | Domperidone | 2   | 0.72 | 1.83 | 3.13 | 4.27 | 20   | L    | H    | 2    |
| 39 | Ebastine    | 2   | 0    | 1.41 | 2.37 | 6.94 | 10   | L    | H    | 2    |
| 40 | Entecavir   | 3   | 1.05 | 2.29 | 2.18 | -2.58| 1    | H    | L    | 3    |
| 41 | Ergotamine tartrate| 1 | 0.79 | 3.69 | 4.6  | 4.66 | 2    | H    | H    | 1    |
| 42 | Erythromycin stearate| 4  | 0.91 | 4.49 | 3.3  | 1.61 | 500  | H    | H    | 1    |
| 43 | Escitalopram| 1   | 0    | 1.08 | 1.87 | 3.13 | 20   | L    | H    | 2    |

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|   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|
|44| Etoposide| 3| 0.6| 3.23| 4.11| 0.03| 50| L| L| 4|
|45| Ezetimibe| 2| 0.81| 1.77| 2.61| 3.96| 10| L| H| 2|
|46| Famotidine| 3| 1.21| 2.78| 2.24| -1.17| 40| H| L| 3|
|47| Febuxostat| 2| 0.57| 1.11| 2.25| 4.4| 80| L| H| 2|
|48| Fexofenadine| 3| 1.2| 2.12| 2.48| 1.96| 180| H| L| 3|
|49| Fosfomycin tromethamine| 3| 0.63| 1.38| 0.98| -0.23| 3000| H| L| 3|
|50| Idebenone| 2| 0.31| 1.56| 0.84| 3.42| 180| H| H| 1|
|51| Indapamide| 1| 0.7| 1.86| 3.2| 2.96| 25| H| H| 2|
|52| Indoramin| 2| 0.57| 1.49| 2.66| 2.84| 25| L| H| 2|
|53| Iopanoic acid| 4| 0.85| 0.74| 2| 4.7| 500| L| H| 2|
|54| Isradipine| 2| 0.13| 1.79| 2.15| 3.92| 5| H| H| 1|
|55| Ivermectin| 1| 0.68| 4.23| 3.21| 5.39| 3| H| H| 1|
|56| Ketoprofen| 2| 0.57| 0.87| 1.97| 2.76| 75| L| H| 2|
|57| Levofoxacin| 3| 0.57| 2.05| 2.58| -0.51| 750| H| L| 3|
|58| Lisinopril| 3| 1.49| 2.47| 2.98| -1.69| 40| H| L| 3|
|59| Lofepramine| 2| 0| 1.35| 2.63| 7.29| 70| L| H| 2|
|60| Lomefoxacin| 3| 0.73| 1.81| 2.37| -0.11| 400| H| L| 3|
|61| Maraviroc| 1| 0.26| 1.75| 2.62| 3.26| 300| L| H| 2|
|62| Memantine| 3| 0.21| 0.66| 0.58| 3.03| 10| H| H| 1|
|63| Mesna| 1| 0.31| 0.92| 1.52| -1.55| 400| H| L| 3|
|64| Methadone| 1| 0| 1.09| 1.72| 4.17| 10| L| H| 2|
|65| Methaqualone| 2| 0| 0.94| 1.74| 3.65| 500| L| H| 2|
|66| Metoclopramide| 3| 0.5| 1.63| 2.31| 2.23| 10| H| H| 1|
|67| Naloxone| 1| 0.5| 1.75| 2.02| 0.16| 2| H| H| 1|
|68| Naltrexone| 1| 0.5| 1.71| 2.03| 0.36| 100| H| H| 1|
|69| Nitrofurantoin| 4| 0.24| 1.34| 2.03| -0.47| 100| H| H| 1|
|70| Nitroglycerin| 1| 0| 0.45| 1.87| 1.76| 0.4| H| H| 1|
|71| Omeprazole| 1| 0.35| 2.05| 3.18| 2.57| 40| L| H| 2|
|72| Oxatremide| 2| 0.33| 1.89| 2.85| 5.62| 30| L| H| 2|
|73| p-Aminosalicylic acid| 1| 0.93| 0.65| 1.48| 1.06| 1200| H| L| 3|
|74| Phenylpropanolamine| 3| 0.46| 1.22| 1.09| 0.58| 75| H| H| 1|
|75| Pitavastatin| 2| 1.2| 1.59| 2.63| 3.59| 4| H| H| 1|
|76| Pravastatin| 3| 1.51| 1.89| 2.11| 2.05| 80| H| H| 1|
|77| Praziquantel| 2| 0| 1.46| 2.42| 3.36| 600| L| H| 2|
|78| Pregabalin| 3| 0.78| 0.97| 0.93| -0.92| 300| H| L| 3|
|79| Quazepam| 2| 0| 0.49| 1.57| 3.2| 15| L| H| 2|
|80| Ramipril| 1| 0.71| 1.96| 2.68| 1.54| 10| H| H| 1|
|81| Ridogrel| 1| 0.57| 1.08| 1.49| 4.54| 5| H| H| 1|
|82| Ritodrine| 3| 1.38| 1.76| 1.83| 1.65| 10| H| L| 3|
### Table 3. BDDCS class changes from initial publication for nine drugs and prediction of BDDCS class in this study

| Generic Name | Listed class\(^a\) | Updated class\(^b\) | Prediction of BDDCS |
|--------------|---------------------|---------------------|---------------------|
| Aliskiren    | 1                   | 3                   | 2                   |
| Clonidine    | 3                   | 1                   | 1                   |
| Colchicine   | 1                   | 3                   | 1                   |
| Diclofenac   | 1                   | 2                   | 2                   |
| Flecainide   | 3                   | 1                   | 1                   |
| Metoclopramide | 3              | 1                   | 1                   |
| Pindolol     | 3                   | 1                   | 1                   |
| Pitavastatin | 2                   | 4                   | 1                   |
| Saxagliptin  | 3                   | 1                   | 2                   |

\(^a\)Ref. [8]

\(^b\)Ref. [34]