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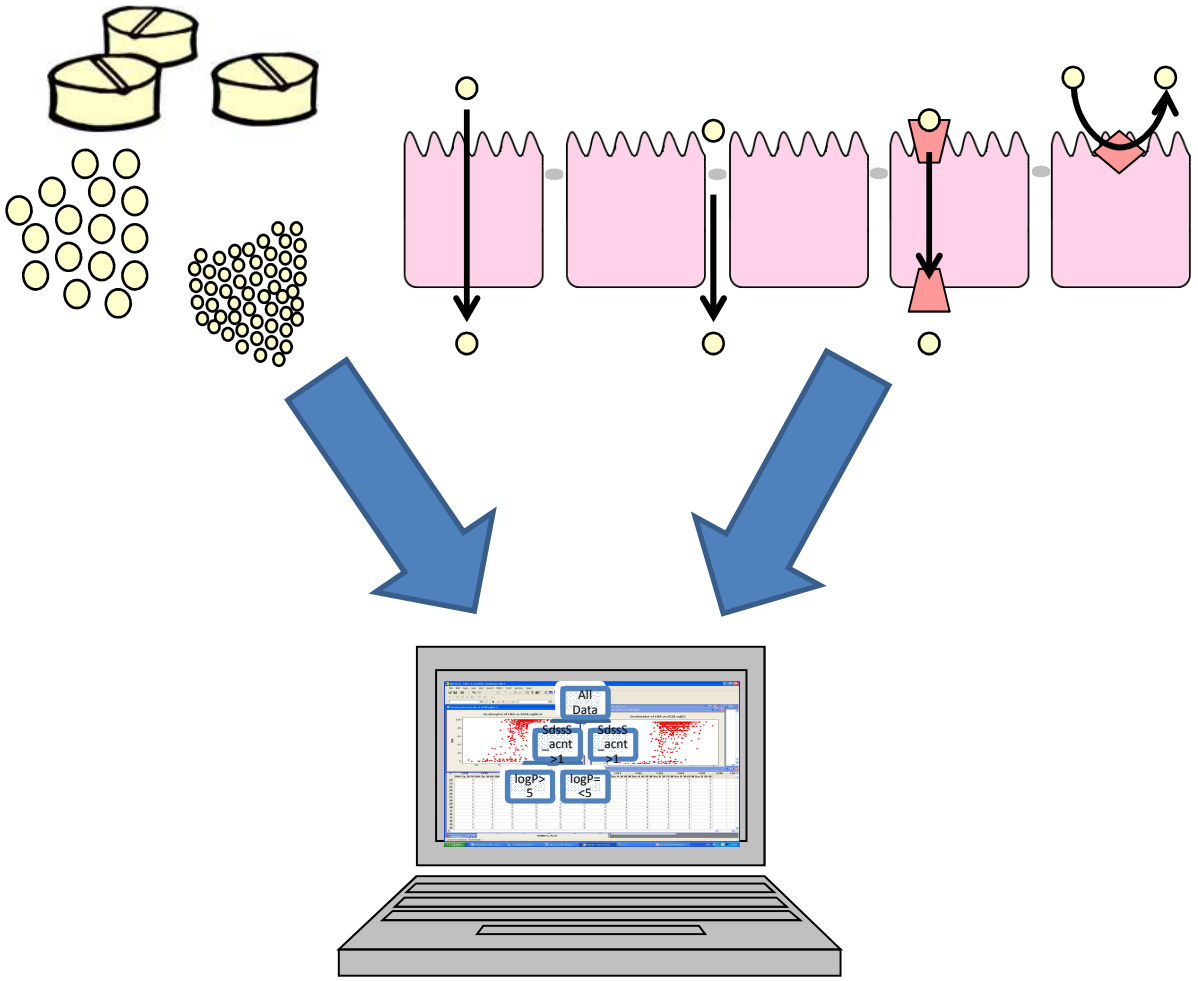

High or Low Oral Absorption

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Decision trees to characterise the roles of permeability and solubility on the prediction of oral absorption

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ABSTRACT

Oral absorption depends on many physiological, physiochemical and formulation factors. Two important properties that govern oral absorption are *in vitro* permeability and solubility, which are commonly used as indicators of human intestinal absorption. Despite this, the nature and exact characteristics of the relationship between these parameters are not well understood. In this study a large dataset of human intestinal absorption was collated along with *in vitro* permeability, aqueous solubility, melting point, and maximum dose for the same compounds. The dataset allowed a permeability threshold to be established objectively to predict high or low intestinal absorption. Using this permeability threshold, classification decision trees incorporating a solubility-related parameter such as experimental or predicted solubility, or the melting point based absorption potential (MPbAP), along with structural molecular descriptors were developed and validated to predict oral absorption class. The decision trees were able to determine the individual roles of permeability and solubility in oral absorption process. Poorly permeable compounds with high solubility show low intestinal absorption, whereas poorly water soluble compounds with high or low permeability may have high intestinal absorption provided that they have certain molecular characteristics such as a small polar surface or specific topology.

KEYWORDS

Intestinal absorption, permeability, solubility, decision trees, QSAR

ABBREVIATIONS USED

%HIA, percentage human intestinal absorption; BCS, Biopharmaceutics Classification System; CART, Classification and regression trees; Caco-2, Human colon adenocarcinoma cell line; FN, false negative; FP, false positive; GSE, general solubility equation; MDCK, Madin-Darby Canine Kidney; MPbAP, melting point based absorption potential; QSAR, Quantitative Structure-Activity Relationship; SE, sensitivity; SP, specificity; TN, true negative; TP, true positive

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1. INTRODUCTION

The assessment of pharmacokinetic properties, especially absorption, is now well established in early drug discovery. The need to determine absorption of new chemical entities is essential for successful orally administered compounds, as well as efficacy, toxicity and other ADME (absorption, distribution, metabolism, excretion) properties [1]. The prediction of oral absorption can be carried out with experimental assays and/or the use of *in silico* models. These experimental and computer models can be used as an indication of intestinal absorption in humans, which is carried out later on in drug development. By testing drug compounds using these models, compounds with undesirable properties can be removed earlier, therefore improving cost effectiveness [2, 3].

Intestinal absorption depends on many physiological, physiochemical and formulation factors. Two important properties that govern oral absorption are permeability and solubility as utilised by the Biopharmaceutics Classification System (BCS) [4]. For a drug to be absorbed it must firstly dissolve in the gastrointestinal fluid in order to then permeate the intestinal membrane. The relationship between these properties is closely, usually inversely, related [5, 6]. As an increasing number of new chemical entities (NCE) have high lipophilicity and low solubility, predicting absorption of NCEs is problematic. Inadequate aqueous solubility can lead to poor, erratic, variable absorption, so it is important to consider the effects of solubility for the prediction of intestinal absorption [7] .

The importance of solubility on oral absorption is highlighted in the literature, but there are few studies that incorporate both experimental solubility and permeability values within a model, in order to see the effect these two properties have on oral absorption [8, 9]. Early oral absorption models are too small to effectively represent all the different biological processes of absorption and the physiochemical properties including solubility [10, 11]. Most studies have removed compounds with solubility issues when modelling oral absorption [12, 13], which is not ideal due to the increasing number of poorly soluble drugs being developed. Zhao and co-workers demonstrated that predicting BCS Class II compounds (low solubility and high permeability) resulted in an overestimation of fraction absorbed by their model [12]. Solubility itself is a complex parameter and in turn dependent on numerous factors, therefore it is important to investigate what multiple elements such as those calculated from the molecular structure may improve understanding of this property in relation to absorption.

Molecular descriptors that describe the process of solubilisation of the drug such as crystal lattice energy, solvent cavity formation energy and solvation energy are utilised in the prediction of solubility [14, 15]. The general solubility equation (GSE) is a simple method that predicts aqueous solubility using only two parameters, logP and melting point [16]. Other methods may employ more specific molecular descriptors to improve the prediction accuracy [17, 18]. GSE and its variants have been used for the estimation of oral absorption-related parameters termed absorption potential [19, 20]. Recently a melting point based absorption potential (MPbAP) has been proposed which is derived from the GSE and includes maximum dose, to give an indication of oral absorption. In general, it was found that the lower the melting point the higher the tendency the compound had to be highly-absorbed and *vice versa*, and it was also found that for higher melting points absorption was limited by dose [21].

Permeability in drug discovery is routinely measured using *in vitro* cell based assays to give an indication of permeability of drug compounds in the intestine, blood brain barrier, nasal cavity and skin [22]. Apparent permeability (P_{app}) is the rate of permeation across cell monolayers and is usually measured in cm/s^{-1}. The ideal permeability model for the small intestine mimics the physical and biochemical processes of intestinal absorption [1]. There are many different cell lines that can be used to measure permeability. Human colon adenocarcinoma (Caco-2) is a commonly used cell line [23-25], which displays biological and characteristic properties of the enterocytes of the small intestine such as the brush border and tight junctions [1, 25-27]. These cells can express a variety of transporters and metabolic enzymes, allowing other transport and metabolism mechanisms to be investigated [28]. Drawbacks of this particular cell line are inter-laboratory differences, variable transporter expression, long culture time, tighter junctions compared with *in vivo* situation and lack of mucus secreting goblet cells [1, 29, 30]. Some of these problems have been resolved by other cell lines such as 2/4/A1, a rat intestinal epithelial cell line, which has leakier tight junctions [31, 32]; also, the cell line HT29-MTX is a co-culture of Caco-2 cells with mucus secreting goblet cells to study the effects of mucus on absorption [33]. Another cell line that has been gaining popularity is MDCK II (Madin-Darby Canine Kidney strain II) cells, due to shorter culture time (of 3-5 days), leakier tight junctions and low expression of transporters compared with Caco-2, making it an ideal cell line for passive permeability assessment even with species and tissue differences [22, 34-36]. There are many similarities and differences

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between Caco-2 and MDCK cell lines. Despite this there is a linear relationship between the two shown using small compound sets [22, 34, 35].

The relationship between permeability and fraction absorption in humans can be determined numerically or categorically. From a classification perspective a permeability threshold indicates high or low intestinal absorption (absorption class). The permeability thresholds defined in the literature vary greatly and the majority of studies appear to set the permeability threshold subjectively from a visual inspection of the graphical fit, rather than using an objective method [13, 37-40]. For example, Artusson *et al* [37], using a dataset of 20 compounds, defined that a compound would have complete absorption if it had a permeability > 1 $x10^{-6}$ cm/s. More recent studies have indicated higher permeability thresholds than 1 $x10^{-6}$ to define a high absorption compound [8, 38, 41]. In a recent investigation, Varma *et al* [36], used Receiver Operating Characteristic (ROC) analysis to objectively define the best permeability threshold for fraction absorbed based on a dataset of 82 compounds with permeability measured in a low transporter expression MDCK II cell line. The threshold defined was > 5 x 10^{-6} cm/s for ≥ 80% or ≥ 90% fraction absorbed. Additionally, the FDA has recommended a set of high and low permeability standards with known fraction absorbed [42]. These standard compounds can be measured alongside NCEs which are then considered as highly or poorly permeable, depending on whether the permeability is greater or lower than the standards; this can then be related to fraction absorbed based on these FDA standards. Potential problems with this are the choice of standard. For example, the high permeability standards propranolol, verapamil and metoprolol have differences in their permeability which could result in potential incorrect prediction depending which standard is used when testing alongside NCEs.

In order to see the effects of solubility and permeability on fraction absorbed, a large dataset is needed. Therefore, the first aim of this work was to expand the permeability dataset by combining data from Caco-2 and MDCK cell lines. By studying the relationship and the effect of different absorption mechanisms between the two cell lines and from the differences already known between the two cell lines, the justification of combining the datasets can be shown. Secondly, the determination of a permeability threshold to predict fraction absorbed class using an objective decision tree method is tested on an external validation set of the permeability dataset collected. Using this permeability threshold, decision trees using experimental and predicted solubility and related properties such as dose number and melting point were included along with structural molecular descriptors to build classification models

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to predict fraction absorbed class. Therefore, the QSAR endpoint is the categorical variable indicating the 'high' or 'low' fraction absorbed class. Based on this work, one can obtain an increased understanding around the relationship between two popular cell based assays and how they can be used to predict absorption class using an objective permeability threshold. In addition, the effect of solubility and related properties on the prediction of fraction absorbed models is explored.

2. METHODS AND MATERIALS

2.1 Datasets

With an extensive search in the literature, multiple datasets were collated consisting of data for human intestinal absorption, transport route, permeability, solubility, dose number, aqueous solubility and melting point. For each compound the name, property value, CAS number, references and additional comments from the authors relating to the data is included and can be found in the **Supporting Information I.** Whenever possible, the original literature was consulted to evaluate data quality. In some cases data from secondary sources was included when original literature could not be located.

2.1.1 Human Intestinal absorption

Intestinal absorption can be assessed and calculated from different types of data such as bioavailability, and urinary and faecal excretion mass balance studies. We used the same principles to calculate and evaluate the reliability of fraction absorbed value as defined by other works [12, 43]. Intestinal absorption values were initially obtained from the published datasets of Hou *et al* [13] and Varma *et al* [43]; this data was scrutinised by checking the original publications. An exhaustive search of the literature was then carried out and additional compounds were also added from the drug information obtained from the FDA Drugs@FDA database (accessed from June 2012 to May 2013) [44]. Where there was no numerical value defined in the literature, categorical values for fraction absorbed were also included for this dataset. At the end, the dataset consisted of 913 numerical and 19 categorical fraction absorption values creating a final dataset of 932 compounds.

2.1.2 Permeability

Apparent permeability (P_{app}) data measured in cm/s^{-1} was collected for compounds with known fraction absorption. The dataset contains apparent permeability data for the two

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different cell lines Caco-2 and MDCK obtained from the literature. The dataset contains 386 Caco-2 and 246 MDCK P_{app} values for drug and drug-like compounds. For 185 compounds the permeability was found for both cell lines, and this dataset was used to investigate the relationship between the two cell lines. Where there were multiple permeability values for a single compound these results were averaged unless they were very different, in which case comparison of MDCK and Caco-2 permeability was carried out (if available) or careful examination of the experimental conditions of the specific value was performed in order to justify inclusion.

For Caco-2 permeability, the published dataset by Pham-The *et al* [45] was used as the starting point from which an exhaustive literature search was carried out. For MDCK permeability, permeability data from two studies by Varma and co-workers [36, 46] were used as a starting point. As there are different strains of this cell line, it was important to reference what strain (if known) was used in the study. In addition, it was decided not to just isolate data collection on one strain, but make a note which would aid in interpretation at a later stage. The main two types of MDCK strains collected were MDCK II and MDCK-MDR1. A preliminary statistical paired t test of these two main strains showed no significant difference between these two strains in this dataset ($p > 0.05$), therefore all the data for MDCK was used together for comparison with Caco-2.

2.1.3 Identification of absorption mechanisms

The knowledge about absorption mechanism will help with interpretation of models and give us a better understanding of the influence of transporter systems on absorption as this is increasingly important in the prediction of drug absorption. For each compound the absorption route was assessed using literature data, review articles and transporter databases. It was recorded if compounds underwent any absorption mechanism other than passive transcellular route. This included carrier mediated systems, such as efflux and influx transporters, and paracellular absorption. A total of 201 (out of 932) were identified to be absorbed via routes other than passive transcellular. It must be noted that, firstly, if no information or evidence was found to suggest alternative absorption mechanisms, this does not necessarily mean it is not a substrate of a transporter or transported via the paracellular route; it may not have been tested and/or results have not been published in the literature. Therefore, in the future we anticipate that this number could increase further when more research is carried out. Secondly, although a compound is identified as a substrate for a

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carrier mediated system, this does not mean that the transport system is the dominating process [47].

2.1.4 Aqueous solubility

Aqueous solubility for 483 compounds in mg/mL was obtained primarily from the AQUASOL dATAbASE (6^{th} Edition) and SRC (PHYSPROP) databases (http://esc.srcinc.com/fatepointer/search.asp) and the literature. Solubility was converted to log molar units (M) and log mg/mL units in this work. For the AQUASOL data, those values that had the highest evaluation codes as defined by the database were selected, and those compounds with more than one value were averaged.

In addition to these values, predicted solubility values were also utilised and compared with experimental in the modelling section of this work. Solubility was calculated by the revised general solubility equation (GSE) using experimental melting point and calculated logP.[16] (**Equation 1** below).

$$\text{Log Sol (GSE)} = 0.5 - 0.01\,(MP - 25) - logP \quad \textbf{(1)}$$

2.1.5 Dose number

Dose number is a dimensionless number used to determine high or low solubility in the Biopharmaceutical Classification System (BCS) [4]. It is calculated using the solubility and maximum strength dose (**Equation 2**).

$$D_o = (M_o / V_o) / S \quad \textbf{(2)}$$

Where D_o is dose number, M_o is the highest dose strength, V_o is 250ml and S is the aqueous solubility (mg/ml). The maximum strength dose was obtained for the compounds in this dataset from the British National Formulary (2012)[48], FDA electronic orange book 2012 (accessed December 2012-January 2013) and Martindale (2009) [49]. Where there were still missing values, an extensive literature search was carried out and the values presented are the authors' best recommendation based on an evaluation of the literature data. Where doses were based on bodyweight, a body weight of 70kg was used to calculate the maximum dose for human.

2.1.6 Melting point

Experimental melting point (in ^{o}C) was obtained from the AQUASOL dATAbASE, SRC (Physprop), the Hazardous substances data bank (HSDB) (http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB) and the literature. The average was taken if a melting point range was stated.

2.1.7 Melting point based absorption potential

The melting point based absorption potential (MPbAP) was derived from the GSE but utilising maximum dose as well as melting point [21]. As shown by **Equation 3** below.

$$\text{MPbAP} = 0.5 - 0.01\,(MP - 25) - \log(4 * Max\ Dose) \quad \textbf{(3)}$$

2.2 Calculated molecular descriptors

Calculated molecular descriptors were calculated from structures using the software packages TSAR 3D v3.3 (Accelrys Inc.), MDL QSAR (Accelrys Inc.), MOE v2010.10 (Chemical Computing Group Inc.) and Advanced Chemistry Development ACD Laboratories/LogD Suite v12. Including the seven descriptors of permeability, solubility and related parameters, a total of 220 molecular descriptors were utilised for analysis.

2.3 Training and validation sets

Using the combined permeability data from the two cell lines yielded an initial dataset of 447 compounds. Compounds with MDCK and Caco-2 permeability data that differed by more than one log unit and one compound that did not have a numerical value for HIA were removed (14 compounds in total). This resulted in a dataset of 433 compounds. The 433 compounds were split into a training set and a validation set. To ensure a similar distribution of fraction absorbed in these two sets, compounds were sorted according to ascending %HIA and then logP values. From each group of six consecutive compounds, five were assigned to the training set, and one compound was allocated to the validation set randomly. The initial training set consisted of 356 compounds and the validation set consisted of 78 compounds.

For models used to determine the influence of solubility and related parameters, compounds that had missing values for solubility, melting point and dose number were removed from the initial training and validation sets. The final compound numbers for decision tree analysis are shown in **Table 1**.

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<<INSERT TABLE 1 HERE>>

2.4 Classification and regression trees (CARTs)

STATISTICA v11 (StatSoft Ltd.) software was used for permeability threshold determination and classification of compounds using CART analysis. CARTs (called C&RT in the STATISTICA software) use decision trees to solve regression and classification problems developed by Breinman *et al* [50]. Hence, in this work the QSAR models are represented as decision trees (a type of graph). According to the observed %HIA values in the data set, compounds were placed into either the "high" class if %HIA was equal to or greater than a specified HIA cut-off (e.g.50%) or the "low" class if %HIA was less than this specified %HIA cutoff. In this work binary classification of (low or high HIA) was carried out using calculated molecular descriptors from the chemical structure, permeability and solubility related parameters. The QSAR models (in the form of decision trees) used in this work were validated by measuring the predictive accuracy of model predictions (prediction of "High" or "Low" oral absorption class) for the compounds in the validation set, as described earlier (section 2.3 – training and validation sets).

Preliminary results indicated that permeability and not solubility was the dominant property selected statistically by CART. Therefore in order to gauge the relative importance of these two parameters, the decision trees were built in two phases. The first phase forced CART to select a suitable permeability threshold for different HIA class definitions. The second phase involved forcing CART to choose thresholds for solubility and related parameters for the second split of the decision tree. After this, CART was allowed to build the remainder of the tree automatically using structural molecular descriptors. These trees were compared with a CART tree developed using the parameters selected automatically by the tree from permeability or solubility parameters or the molecular descriptors provided.

2.5 Permeability threshold determination using CART

The permeability threshold is the numerical value chosen by CART that best predicts HIA class. In this work several different analyses were performed where high absorption compounds were defined as those having HIA values of above 30, 50, 70, 80 or 90%. Using the training set of 356 compounds, HIA class was used as the dependent variable and permeability as the independent variable. The CART analysis was restricted to only one split

to give the permeability threshold. This threshold was tested using a validation set of 78 compounds. Due to the class imbalance, where there are many more highly-absorbed than poorly-absorbed compounds, higher misclassification costs were applied to false positives to overcome this bias. Based on previous works the use of misclassification costs has shown improved model accuracy [51]. The misclassification cost values applied depended on the class distribution of the dataset. For instance, when the "high absorption" class is defined as having %HIA ≥ 30%, the cost of a false positive was considered five times the cost of a false negative due to roughly five times more highly absorbed compounds in the data set. Misclassification costs of 5, 4, 3, 2.5 and 2 were applied to false positives in the analyses where the high HIA class had been defined as those compounds having %HIA values equal or above 30, 50, 70, 80 and 90%, respectively.

2.6 Permeability and solubility related model analysis for oral absorption class determination

In this section, models were built using HIA class as the dependent variable where high absorption was defined as HIA ≥ 80% and molecular descriptors were utilised as the independent variables for model building. The HIA class definition of ≥ 80% was selected based on preliminary work, where when using lower HIA class definition such as 30-70% due to the lower number of poorly absorbed compounds only poor models could be achieved. Using a higher threshold of 90% resulted in poorer overall accuracy (based on preliminary analysis), and this threshold is too high to predict oral absorption class effectively with a high number of false negatives.

In this work permeability was set as the first split variable and two alternative approaches were used to choose the remaining split variables. In the first one, the CART tree was allowed to grow automatically. In the second one, each of the solubility and related parameters (dose number and melting point) were manually chosen as then second split variable (note that CART still chooses the cut-off point automatically) and then the tree was allowed to grow automatically. Stopping factors were used to prevent overfitting of the CART trees and was the minimum number of compounds for splitting. This was set at 11 for the permeability only CART trees and eight for permeability and solubility trees.

2.7 Statistical significance of the models

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To determine the relationship between Caco-2 and MDCK permeability, MINITAB Statistical Software (version 16.1.1.0) and Prism (GraphPad Software, Inc) v.5.02 were used to carry out linear regression, identify outliers and perform statistical significance testing between the different absorption mechanisms. For linear regression the parameter reported to assess the fit of the two variables was the squared correlation coefficient, r^2 forced through the origin. For correlation analysis the Pearson's correlation coefficient and the Spearman's ranking correlation coefficient (r_s) were calculated. It must be emphasised here that r^2 based on the regression line forced through the origin is not comparable to r^2 values where the regression line is not forced through the origin [52]. The statistical significance of the correlations and regression lines and comparison of the regression lines for different absorption mechanisms (using the intercept and the slope values) was depicted by p values. P values <0.05 indicated significance.

The predictive performance of the classification models built using CART in this work was measured using sensitivity (SE), specificity (SP) and SP × SE. Sensitivity is the ratio of correct classifications for the highly absorbed compound class (SE = TP/(TP + FN)), where TP is the number of true positives and FN is the number of false negatives. Specificity is the ratio of correct classifications of poorly absorbed compounds (SP = TN/(TN + FP)), where TN is the number of true negatives and FP is the number of false positives. In this work overall accuracy is defined by specificity multiplied by sensitivity (SP × SE). This measure represents the overall predictive performance of both high and low class prediction. In addition, this measure will not be overly influenced by the classification accuracy of the majority high absorption class, and it has been used in previous investigations [51, 53].

3. RESULTS AND DISCUSSIONS

In this work in order to investigate the effects of permeability and solubility a large dataset of human intestinal absorption was gathered from the original literature and then for the same compounds Caco-2 and MDCK permabilities, solubility, melting point and dose were gathered from the original literature. **Table 2** shows the collated data which is available in the **supporting information I**, where n denotes the number of compounds for each property. This data was used in order to develop models for predicting high/low oral absorption and to explore suitability of different solubility and permeability measures from different sources as descriptors of intestinal absorption.

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<<INSERT TABLE 2 HERE>>

In terms of permeability, we have gathered permeability measured in both Caco-2 and MDCK cell lines. *In vitro* permeability through different cell lines is commonly used as a high throughput measure of effective intestinal absorption in early drug discovery. Other cell lines such as MDCK, 2/4/A1 and HT29-MTX have also been used to assess compound permeability. There have been a few studies, which show the linear relationship between these cell lines. For example, Braun *et al* [22] studied the relationship between Caco-2 and MDCK cell lines and from 14 compounds achieved an r^2 of 0.86. However, Adveef *et al* [35] achieved a r^2 of 0.90 using a dataset of 79 compounds.

3.1 Comparison of Caco-2 and MDCK apparent permeability as indicators of intestinal absorption

For 185 compounds, the *in vitro* apparent permeability from both Caco-2 and MDCK cell lines was obtained from the literature. By an exhaustive literature search transport routes were identified for all these compounds. Plotting the permeability of these two cell lines on a log scale a linear relationship is shown (**Figure 1**) where the transport routes have also been highlighted. Out of 185 compounds in this figure, 96 compounds were found to be substrates of a transporter system and 11 compounds have been suggested to be absorbed to some extent via paracellular route.

<<INSERT FIGURE 1 HERE>>

It can be seen in the plot that Caco-2 and MDCK permeability of majority of compounds regardless of their absorption routes correlate well with each other. However, there are compounds that deviate significantly from this line and removal of 9 outlier compounds (compound names shown in the **Figure 1**) improves the correlation significantly (**Table 3**). Details of the outlier compounds and a description of reasons can be found in **Supporting Information II**. A better linear relationship between the two cell lines is also achieved when only compounds undergoing passive transcellular absorption are plotted (**Table 3**). It may be noted in **Table 3** that the correlation between the cell lines are better after the removal of 9 outliers than after the removal of all the compounds with a transporter effect. It is also noteworthy that not all the outliers were substrates of a transporter; examples are phenazopyridine and glipizide where no transport system other than passive-transcellular has

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been identified. Both these drugs have poor solubilities (dissolution limiting solubility) and classed in Class II of Biopharmaceutics classification system (BCS) [54, 55].

Similar conclusions can be made from the results of previous studies where transporter mediated effects could not be identified by correlating the permeability through different cell lines. Irvine *et al* [34] compared the apparently permeability of 55 compounds using MDCK and Caco-2 cells. This study achieved an r^2 of 0.79. Irvine identified 12 compounds that were substrates for carrier mediated systems. We crossed referenced the remaining compounds used by Irvine with our database and identified an additional 18 compounds to be substrates for carrier mediated systems. Therefore over half of this original dataset has now been found to be affected by a carrier mediated route. The 12 compounds highlighted as undergoing carrier systems in most cases were within the linear fit of Irvine's, with only a few exceptions. The explanation by Irvine of why known P-gp substrates were not identified in comparing the two cell lines is not suitable. For the P-gp substrates highlighted in the work, it was stated the reason they could not be identified was due to saturation of the transport mechanism in the assay. Braun *et al* [22] used the same compounds but at lower concentrations, and they were still unable to identify known P-gp substrates. It was concluded that using the relationship between MDCK and Caco-2 could not identify P-gp substrates. From this work the correlation between MDCK and Caco-2 permeability does indicate the same result that compounds with carrier mediated mechanisms do not deviate from the correlation between Caco-2 and MDCK permeabilities. This is despite the fact that the transporters have different abundance levels in these two cell lines.

<<INSERT TABLE 3 HERE>>

We have complied a table that compares the cells and small intestine in terms of species origin, tightness of the cell junctions and also the transporter and enzyme expressions (**Table S1 in Supporting Information III**). One thing to note is the lack of information/evidence in the literature for transporter and enzyme expression especially for the specific strains of the MDCK cell line, which is less well studied. For the small intestine the expression of transporters and enzyme systems can vary from the three sections of the small intestine, as compounds are not just absorbed from one section, we tried to accommodate an overview of expression from the human small intestine [56]. It can be seen from **Table S1** that the main differences between MDCK and Caco-2 cell lines in general are that MDCK does not express some transporter types and that MDCK has a lower abundance of some of the other

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transporters compared to Caco-2 cell lines. However it must be noted that expression of transporters or enzymes does not necessarily correlate with their functionality for affecting the absorption of the compounds across different membrane/cell lines [57, 58], and as it was shown earlier, most substrates of different transporters do not deviate from the correlation between Caco-2 and MDCK permeabilities.

The different expression levels of metabolising enzymes in the different cell lines could also potentially affect the permeability of compounds. The expression and activity of CYP3A4 enzymes in Caco-2 cells are either not present or very weak [30, 59]. A recent investigation has found no evidence of CYP3A4 expression in MDCK II cells [60]. Unfortunately the lack of information regarding enzymatic activity in the cell lines makes it difficult to comprehensively compare and contrast the suitability of these *in vitro* tools as indicators of intestinal absorption.

Cell based assays, particularly Caco-2, have a reputation for variability. The differences can arise from the experimental conditions, which in turn can affect the monolayer, those that affect the analysis of samples and also the physiochemical properties of the compound [61]. A good example is solubility, which depending on experimental conditions can cause variation particularly for compounds with low solubility such as the outlier compounds phenazopyridine and glipizide [54, 55] (**Figure 1**).

The prime purpose of cell based assays such as Caco-2 and MDCK is to study the rate of passive permeability rather than other transport routes involving influx and efflux transporters. In this dataset, out of the 185 compounds, 96 were identified as undergoing transport routes other than passive. In some cases, more than one route was identified as being involved for the transport of the compound **(Table 4).**

<<INSERT TABLE 4 HERE>>

From **Table 4**, there are a higher number of compounds identified as carrier mediated efflux substrates compared to influx substrates. The majority of compounds that were identified as efflux substrates are substrates of the P-gp transporter, which is always tested due to the great influence this transporter has on reducing absorption of many compounds.

We compared the permeability values obtained from Caco-2 and MDCK cell lines for all compounds and subgroups of compounds showing specific routes of absorption as described

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in **Table 4**. Two statistical methods were employed; 1) paired student t-test to compare MDCK and Caco-2 permeability values of a subgroup of compounds, and 2) comparison of the coefficients of the correlation lines of subgroups of compounds, e.g. efflux substrates and compounds with passive transcellular absorption. The results for subgroups indicated that permeabilities through MDCK and Caco-2 cell lines are correlated with similar slopes and intercepts for compounds with different absorption mechanisms (**Figures S1-S7 and Table S2** in the **Supporting Information III**). The only significant difference between the correlation lines was the difference between compounds undergoing transcellular and paracellular absorption routes (p value 0.0023). However, despite the different tightness of the Caco-2 and MDCK cell lines, the observed difference may be due to the narrow range of permeability values of the compounds with paracellular absorption route resulting in a non-significant correlation between MDCK and Caco-2 solubility of this subgroup (**Figure S1 in Supporting Information III**). This hypothesis is supported by the results of a paired student t test between the permeability values of the two cell lines for the 11 compounds undergoing paracellular absorption (as a main or shared transport route) showed no significant difference between Caco-2 and MDCK permeabilities ($p > 0.05$). In addition paired t tests for all different absorption mechanism groups and no significant differences between the two cell lines for these absorption groups were found. Therefore, we can conclude that in general there are no statistically significant differences between the two cell lines even when considering separately the compounds with different absorption mechanisms. Therefore, the data from both these cell lines can be combined into a larger permeability dataset for use in further modelling.

3.2 Determining permeability threshold for an effective oral absorption

In this work we use the large dataset of combined Caco-2 and MDCK permeability and a statistical method (CART) to identify statistically valid permeability threshold for high/low oral absorption. Using CART analysis, a permeability threshold value was obtained to predict the high or low intestinal absorption (HIA class) using a training set of 356 compounds. Several different analyses were performed where high absorption compounds were defined as those having HIA values of above 30, 50, 70, 80 or 90%. In order to optimise the threshold selection, various CART models using different misclassification cost ratios for false positives: false negatives (FP:FN) were generated [51, 53]. The results below show the permeability threshold selected by the CART analyses and the accuracy, specificity and sensitivity of the class prediction (**Table 5**).

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<<INSERT TABLE 5 HERE>>

It can be seen in **Table 5** that using high ratios of (FP:FN) misclassification costs results in improved accuracy of the permeability threshold for classification of compounds into high or low absorption groups for all definitions of HIA class. For example using equal misclassification costs to find permeability threshold for dividing compounds into ≥ 30% or < 30% HIA is not successful at all (**Model 1 Table 5**) but increasing the cost of false positives to five times that of the false negatives results in a high accuracy of classification and a robust threshold of -5.98 (in log units) (model 6). It must be noted here that different high/low definitions of HIA result in different proportions of compounds in "high" or "low" absorption classes, and hence the choice of misclassification cost ratios to reflect the ratios of highly absorbed to poorly absorbed compounds [51, 53]. Therefore by applying higher misclassification costs to reduce false positives, this has shifted the permeability threshold in order to reduce the number of false positives due to the under representation of the poorly absorbed class (**Figure 2**). The one exception to this is the 80% HIA class definition, where applying misclassification costs had no effect on the permeability threshold. In practice, when using the permeability threshold to classify high/low absorption compounds, the suitable threshold suggested by models 6-10 can be used for HIA class definition. The permeability thresholds determined by CART when applying higher misclassification costs from **Table 5** can be shown below (**Figure 2**) when plotting fraction absorbed against permeability for the training and validation sets.

<<INSERT FIGURE 2 HERE>>

As can be seen by **Figure 2** there is a correlation between fraction absorbed and permeability. It is common in the literature to assume a sigmoid fit to the relationship between HIA and permeability [32, 36, 62]. However, there are too few points at the lower plateau region to justify fitting a sigmoidal fit from statistical point of view; in spite of this we found a r^2 of 0.435 for a sigmoid fit to the whole 433 compounds. The collection of more data in the 0-50% region may resolve this problem.

From **Figure 2,** there are compounds that are highly absorbed but have permeability values below the threshold and *vice versa*. The most pronounced outliers have been shown in the figure (**Figure 2**) using boxes A and B. Compounds with low permeability but high fraction absorbed (Region A on **Figure 2**) have been identified as mainly highly soluble and substrates for influx carrier mediated transporters. Examples of these are ribavirin and

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lamivudine [63, 64]. Due to the lower levels of these transporters, particularly PEPT1 *in vitro*, the cell permeability underestimates the percentage absorbed of this set of compounds. On the other hand, compounds with high permeability but low fraction absorbed tend to be those that are susceptible to gut metabolism and poorly soluble from this dataset (Region B on **Figure 2**). Examples of compounds in this outlier group are lovastatin and tacrolimus [65, 66].

Although the liver is the main metabolising organ, gut metabolism can contribute significantly to overall metabolism and should be considered [67]. Compounds susceptible to gut metabolism, specifically CYP3A4 substrates, are highly permeable *in vitro* but are poorly absorbed *in vivo.* However there are other CYP3A4 substrates in this dataset which do not appear to undergo extensive gut metabolism so are both highly absorbed and highly permeable. Reasons for why some compounds are susceptible to gut metabolism and others are not even though they are both CYP3A4 substrates could be due to the different biotransformation rate by this enzyme, solubility/ dissolution rate, permeation rate, dose amount and substrate affinity [67-69]. A list of these compounds in regions A and B in **Figure 2** can be found in the **Supporting Information II**.

3.3 Oral absorption prediction using solubility, dose number and melting point

From **Figure 2,** we have identified potential outliers in the relationship between oral absorption and permeability. Using the models built with permeability and solubility parameters and molecular descriptors, these misclassifications could be classified correctly due to the influence of solubility and other related parameters on oral absorption. For example, false positives are highly permeable compounds with poor oral absorption. These compounds maybe poorly soluble compounds or those undergoing gut metabolism.

CART classification models to predict highly absorbed or poorly absorbed class of compounds (HIA $\geq$ 80 or < 80%) were built using the training sets described in the material and methods section. The permeability for $\geq$ 80% absorption (at -5.15 log scale according to **Table 5**) was used to develop the models. The 80% class definition was chosen as when using lower HIA% values to define high or low absorption led to very low number of poorly absorbed compounds, compared with highly absorbed compounds which would seriously reduce significance of models. The HIA 90% cut-off for class definition, although used in some previous work, was not chosen in this work as (based on our preliminary analysis) that definition resulted in poor overall accuracy in the produced models, and the 90% threshold is

too high to predict oral absorption class effectively. Selected CART models produced for the prediction of HIA class (HIA> or ≤80%) using permeability and solubility related parameters and molecular descriptors are shown in **Table 6**. Note that for all models permeability was always used as the first split variable and the table gives the variables used for the second splits. After the second splits, CART picks the most significant parameter out of all the molecular descriptors and physicochemical properties available. In **Table 6**, in model 1 after permeability as the first split variable, CART automatically builds the rest of the tree by selecting the most significant property/molecular descriptor. For models 2-4, solubility; calculated solubility (GSE method or melting point based absorption potential (MPbAP)) were used on both (high and low permeability) sides of the tree for the second split, and after this CART automatically built the rest of the tree. Models 5-10 were built using different combinations of solubility and related parameters on either the high or low permeability side of the trees. Finally, models 11-12 were combinations of the molecular descriptors and solubility related parameters in high or low permeability sides of the trees.

<<INSERT TABLE 6 HEERE>>

From **Table 6** it is interesting to note which properties were used to build the selected models. Note that many combinations of melting point, dose and solubility related parameters were tested and **Table 6** is a selection of the best models based on accuracy (SE X SP). Using melting point did not yield high prediction models (data not shown). It was thought that due to the relationship between melting point and solubility this parameter might be a useful alternative to solubility, as these two properties share similar functions such as enthalpy energies which must be overcome in order to solubilise or melt. Additionally, dose number was useful only for splitting the high permeability compounds and the combination with MPbAP yielded for a good prediction model (Model 6 in **Table 6**). Dose number is used to define high and low solubility for the BCS system [4, 42]. By definition, increasing the dose or a low solubility will result in a high dose number and this is expected to lead to poor oral absorption of highly permeable compounds.

The majority of the selected models in **Table 6** incorporate solubility and predicted solubility especially for highly permeable compounds. Unlike GSE solubility which was used on both sides of the CART trees, MPbAP only yielded good models when used for splitting on the high permeability compounds. Experimental solubility in two units, mg/ml or molar, have been used in models. Solubility in M, which takes into account the molecular weight and is

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smaller for high molecular weight compounds, was utilised for splitting of the low permeability compounds (Models 8, 9 and 10).

In terms of the role of solubility in the absorption process, one would expect poor absorption of poorly soluble compounds, due to solubility being the rate limiting factor in absorption. However, this is not the picture presented by the classification trees 1-12 (**See Supporting Information III**). According to the classification tree models, the low permeability and high solubility compounds always have low intestinal absorption (< 80%). This is probably due to the highly polar nature of such compounds. On the other hand, poorly water soluble compounds of low permeability may be highly absorbed from the small intestine if they have small polar surface area (models 3-7) or a small sum of absolute atomic partial charge, ABSQ (models 2, 8, 9, 10), which also indicates polarity of molecules. The absorption limiting effect of poor aqueous solubility is not seen for highly permeable compounds either. Here, highly permeable compounds with poor aqueous solubility are still highly absorbable from GI, with the exception of compounds with high polar surface area, low dipole moment (models 2, 5, 9) or small Balaban Topological index which is an indicator of molecular shape (models 3, 4, 10, 11). The reason for not observing the limiting effect of poor aqueous solubility here could be firstly the lack of enough representation of these solubility limiting compounds in the dataset and secondly the effect of formulation of oral dosage forms with measures taken for improved dissolution rate (excipients, particles size, etc) which could mask previous solubility limiting effects of such compounds.

The top molecular descriptors used in models 1-12 in **Table 6** are polar surface area (PSA) and Balaban topological index. Both of these descriptors are related to both absorption and solubility prediction models [70, 71]. PSA is the area of the van der Waals surface that arises from oxygen and nitrogen atoms or hydrogen atoms bound to these atoms [70]. The Balaban topological index, *J*, is the average-distance sum connectivity and relates to the shape of the molecule [72]. The next popular descriptors are sum of absolute charges on each atom of the molecule (ABSQ) and lowest unoccupied molecular orbital energy (LUMO) calculated by VAMP [73].

3.4 Selected CART models

In order to generally compare models 1-12 from **Table 6**, the compound datasets used to build the resulting models should be taken into account. The degree of difficulty of the classification model will change depending on the compounds in the dataset. When the

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dataset is large, e.g. in the case of model 1, there are more compounds that maybe harder to classify in the dataset. The model with the highest SP x SE for the validation set is model 8, with a value of 0.697; however this is based on a training set of only 197 and a validation set of 40 compounds due to the missing experimental solubility or melting point values. On the other hand, model 12 has a slightly lower SP x SE of 0.682 for the validation set, but it was built using a training set of 257 and assessed using a validation set of 51 compounds; therefore it may be more suitable for generalization ability for new compounds, as it covers a wider chemical space compared with model 8. Moreover the only experimental parameter used in this model is melting point that is used for the calculation of MPbAP. We also selected model 7, which has used calculated solubility and MPbAP, and model 3 which has used only the calculated solubility to indicate the roles of solubility and absorption potential. The CART models are presented in **Figures 3-5**. Brief description of molecular descriptors has been presented in **Supporting Information III (Table S3)**.

<<INSERT FIGURE 3 HERE>>

In **Figure 3**, Model 3, permeability is used as the first CART split variable and then calculated solubility from GSE equation on both sides of the tree was used as the second split variable. Polar surface area and Balaban index were picked automatically by the CART analysis. The model shows that highly permeable and highly soluble compounds have high intestinal absorption (node 7). Moreover, compounds with low predicted solubility (≤-4.74) can still be classed as highly absorbed if the Balaban index is > 1.57. Compounds with a low Balaban index will be poorly absorbed and such examples include mebendazole and ketoconazole. In spite of this there are misclassifications in this node 8 in Figure 3; ziprasidone and tiagabine are misclassified as poorly absorbed when in fact they have HIA ≥ 80%. Balaban topological index, J, a highly discriminant topological descriptor, gives an indication of shape including branching and cyclicity of a molecule. A high index can indicate a high number of branches, close proximity of the position of these branches, as well as increased number of double bonds on a molecule. A low index can indicate a low level of branching as well as a larger number of cyclic groups [72]. The relationship between Balaban index and solubility with reference to melting point has been shown previously in the literature [15]. In spite of this there is not much difference between the calculated GSE solubilities between the two nodes although there is a significant difference betwee the

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average melting points (222 ^{o}C compared with 193 ^{o}C in nodes 8 and 9 respectively), suggesting a possible effect of melting point on absorption.

Poorly permeable compounds are highly absorbed only for compounds with predicted solubility ≤ -1.12 if the PSA is low. This is a higher solubility value than the threshold seen in splitting of node 3, and is not expected to limit the intestinal absorption. There are some misclassified compounds in this group, which are actually poorly absorbed despite having a low PSA, therefore classified as highly-absorbed according to this tree. The reasons for misclassifications is mostly due to efflux mechanisms reducing the absorption of compounds and examples include nadolol and norfloxacin which both have low PSA and classed as highly absorbed but are observed to have poor oral absorption due to transporter effects [31, 74]. Unlike nadolol which is classed as highly soluble, norfloxacin is considered as a poorly soluble compound in class IV of the BCS system. One may speculate that presence of more such compounds in this dataset, may have led to further split of this node based on solubility to class compounds with extremely low aqueous solubility as poorly soluble.

<<INSERT FIGURE 4 HERE>>

Model 7 was built using GSE solubility for the second split of the poorly permeable compounds (node 2) and MPbAP for the second split of highly permeable compounds in node 3. This model was chosen due to high validation SP x SE using a larger training and validation set. The descriptors used in this tree are the same as in **Figure 3**. Model 3, however, using the split based on MPbAP appears to split more compounds into node 6 to be classed by Balaban topological index. In this tree a lower threshold of 1.54 for Balaban Topological index increases the number of correctly classified poorly absorbed compounds when permeability is high examples of this type of compounds include the BCS class II compounds spironolactone and ketoconazole.

<<INSERT FIGURE 5 HERE>>

From **Figure 5** classification of highly permeable compounds in node 3 is the same as Figure 4. Poorly permeable compounds with a high number of hydrogen bonding donors (SHHBd >6.61) will be poorly absorbed, which is confirmed by the literature such as Lipinski's rule of five, where compounds are likely to be poorly absorbed if two or more of the following rules are broken: more than > 5 hydrogen bond donors, > 10 hydrogen bond acceptors, logP > 5 and molecular weight > 500Da [75]. Compounds can be misclassified as poorly absorbed

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based on a higher number of hydrogen bond donor groups mainly due to being highly absorbed due to substrate specificity for influx transporters. Examples of misclassified compounds include ribavirin and folinic acid.

A poorly permeable compound will still be highly absorbed if HOMO energy is greater than -8.76. A comparison of the molecular structures in this node indicates that these compounds have more aromatic rings compared with compounds with lower HOMO energy (node ID 8) where the average number of aromatic rings is one. In addition it was also found that a number of low HOMO compounds had a permanent quaternary ammonium or ionisable centre such as trospium and neostigmine.

Even if a poorly permeable compound has a low HOMO energy it can still be classed as highly absorbed if the compound has few methyl groups (SsCH3 $\leq$ 3.509) or log P > 1.239. Compounds with logP < 1.24 are classified as poorly absorbed, but there are false negatives such as orally administered cephradine and baclofen, which are both highly absorbed but are predicted as poorly absorbed by having a low logP. The reason for some of the false negatives in this node is that some of these compounds are substrates for influx carrier mediated systems.

3.5 Discussion of related literature

3.5.1 Subjective definition of a permeability threshold for oral absorption prediction

Permeability from *in vitro* cell based assays has been utilised frequently in the literature. These thresholds are then used to give an indication of potential oral absorption from permeability data. A summary of a few permeability thresholds defined by other works is shown in **Table 7.**

<<INSERT TABLE 7 HERE>>

Early permeability thresholds defined by works in the literature are based on small compound datasets. Artusson *et al* [37] set a permeability threshold of > 1 x 10^{-6} cm/s for complete absorption based on 20 compounds. Based on other works in the literature this value is too low to predict complete absorption, where other works have permeability thresholds one order of magnitude higher. For example, from **Table 7**, Yee *et al* [41] has stated > 10 x 10^{-6} cm/s permeability is related to absorption > 70%. What is apparent is the difference between permeability thresholds from different sources, which is dependent on the small number of

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compounds tested and inter and intra laboratory differences [13]. In comparison, our permeability thresholds are statistically defined by CART rather than a subjective determination; the thresholds picked by CART are similar to those in the literature, especially when high absorption was set at either as > 70%, > 80% or > 90%, indicating that high absorption is related to permeability > 7 x 10^{-6} cm/s. The permeability threshold determined by Hou *et al* [13] of 6 x 10^{-6} cm/s is based on data from numerous sources and is very similar to our 70 - 90% class permeability thresholds.

Di *et al* (2011) [40] used MDCK II cells with low efflux endogenous transporter expression (MDCK-LE) to define a threshold of 3 x 10^{-6} cm/s to distinguish between low/medium absorbed compounds (< 80% HIA) and highly absorbed compounds. A dataset published by Varma *et al* (2012) [36] using the MDCK-LE cell line shows that the permeability threshold defined ROC analysis using this cell line (≥ 5.0 x 10^{-6} cm/s) is similar to Caco-2 thresholds in the literature, and this value is in agreement with CART permeability thresholds in this work. The threshold similarity between Caco-2 and MDCK cell lines is expected by the linear relationship between these two cell lines shown in this work.

Finally more recently Pham-The *et al* (2013) [62] established a rank order relationship between Caco-2 permeability and oral absorption for 324 compounds. The thresholds defined were based on standard compounds from the FDA with known fraction absorbed values. For example, for a compound to be considered highly absorbed, it must have an apparent permeability greater than metoprolol, a FDA standard compound with known HIA. In this case Caco-2 permeability greater than 16 x 10^{-6} cm/s, which is 0.8 times the metoprolol permeability was used to take into account the lower HIA threshold of 85% used. For the low absorption threshold an average value of 0.7 x 10^{-6} cm/s, based on the permeability of mannitol was used. In this study this threshold was to define compounds with HIA < 30% however mannitol has a reported HIA of ~18% therefore the use of this permeability threshold may increase the number of false negatives.

3.5.2 The influence of permeability and solubility on oral absorption modelling

Permeability and solubility are two important factors important for oral absorption. Therefore the effect these two properties have on oral absorption and in turn how they influence oral absorption prediction is important to establish. From the literature there is a lot of focus on permeability and as shown in this work there is a rank order relationship between HIA and permeability. On the other hand, solubility seems not to be regarded as important as

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permeability in relation to oral absorption, but as a factor that can lead to poor (solubility limited) absorption in addition to other limiting factors such as transporter and enzyme effects. Furthermore, the relative importance of solubility could be dependent on the research organization and the mechanistic importance of solubility in regards to oral absorption may not be considered [6]. In spite of this the main reasons for poor oral absorption have been shown to be either poor permeability or poor solubility or both [76].

The results of this work indicate that permeability is the most important parameter influencing oral absorption prediction. Permeability was always picked as top molecular descriptor when building CART models. In contrast, solubility and the related parameters were never picked as the top descriptor or even in the second split, unless selected manually at this second level in order to examine if there was any influence of solubility on oral absorption prediction.

It is apparent that solubility can be a rate-limiting step in oral absorption [4, 12, 77]. This is based on the principle that a drug must be dissolved in the gastrointestinal fluid in order to then permeate the membrane to be absorbed. However formulation development strategies can overcome this problem, for example by employing solubilising agents, pH control, or complexation [78].

In any case, the results obtained here do not directly indicate the poor absorption of poorly soluble compounds and the effects of poor solubility in limiting absorption. According to this study, in general compounds that are highly permeable but have low solubility can be predicted as highly or poorly absorbed depending on the other molecular properties. Moreover, poorly permeable but highly soluble compounds are classed as poorly absorbed, although there are exceptions to this i.e. the false negatives. One important consideration in analysing these results is the threshold of solubility in the models. For example, poorly permeable compounds with poor solubility may have high oral absorption (see models 3 and 7 for example). However, it must be noted here that poor solubility has been defined as <-1.12 in log unit, which is quite high when comparing with the threshold values suggested in the literature for BCS classes II and IV [4]. A further observation from the models could be the poor representation of very poorly soluble compounds in the dataset i.e. those having solubility-limited absorption. As a result, it may not be statistically advantageous to further split the classification tree to allocate these compounds into a separate terminal node. For example in a large dataset of fraction absorbed, 24 were highlighted to have solubility issues

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772 out of 648 compounds[13]. Besides this the formulation techniques may improve the
773 dissolution rate of these compounds and overcome the low solubility issues of compounds in
774 the fraction absorbed dataset used in this work.

775 It is difficult to directly compare other models in the literature with this work, as different
776 data sets and methods have been used. Early oral absorption models which use a diverse
777 dataset are too small to represent all the different biological processes of absorption and other
778 factors such as solubility. The majority of oral absorption models in the literature do not
779 include compounds which have solubility issues [10, 79]. Therefore, these and other models
780 may only be useful for predicting absorption for compounds with no solubility issues. In
781 addition, some of these studies also removed compounds with transporter effects or
782 compounds with a permanent charge [13, 80]. This simplifies the resulting models by
783 removing those compounds with these rate-limiting steps. However, the main issue with this
784 is the potential impact on the generalizability of the resulting models which will fail to
785 predict the oral absorption of these excluded compound classes despite the increased need in
786 current drug discovery projects for prediction of absorption of the increasingly poorly-soluble
787 compounds.

788 In studies by Zhao and co-workers, data with solubility and dose dependency was defined
789 and not used in the majority of the initial models. However upon inclusion of these
790 compounds with solubility issues the resulting models had higher error [81]. It was also noted
791 however that the more insoluble a compound the lower the resulting absorption. In a later
792 study compounds identified with no solubility issues were used to built models and some of
793 these resulting models were then used to predict absorption for the compounds with dose-
794 limiting and dose dependency effects. Overall prediction of absorption of these excluded
795 compounds was in agreement with observed values or the models tended to overestimate
796 absorption [12]. Our oral absorption models are able to predict oral absorption class even
797 with poor solubility for majority of compounds by incorporating molecular descriptors in
798 addition to permeability and solubility into the models. From the list of 27 compounds with
799 solubility and related problems defined by Zhao *et al* (2001) [12], 14 were utilised in this
800 work with experimental permeability and solubility values present. Using the best models
801 chosen, 11 out of 14 compounds were predicted correctly by model 3, 12 out of 14 correct
802 predictions by model 7 and all 14 compounds were predicted correctly using model 12.

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With the extended use of BCS classification in drug discovery, the influence of solubility and permeability is of great interest [82]. In work by Pham-The et al (2013), oral absorption was predicted, taking into account solubility, which is a general aim of the BCS. In this study, Pham-The, using a rank order relationship, noted that the relationship between permeability and oral absorption is less certain for poorly absorbed compounds which is a similar observation to our results. They also found various contour plots that incorporating solubility improves classification of HIA based on permeability data by about 10%; therefore showing that potentially using solubility in models is advantageous for oral absorption prediction.

From the literature examples as well as this work the influence of solubility could be included to help predict oral absorption. However the main issue is the lack of experimental solubility for drug compounds to be used in oral absorption modelling. The use of experimental solubility data in the prediction of oral absorption alongside permeability yields good accuracy to predict oral absorption however the lack of experimental solubility limits the application for the prediction of new compounds. Therefore, according to our results, predicted solubility such as GSE solubility and parameters such as MPbAP can be used successfully instead of experimental solubility. These are based on simple properties of lipophilicity, melting point and dose. Despite this, melting point alone was not successful in providing an adequate alternative to experimental solubility, even though partition coefficient was also available to be used concurrently in the same model. Due to the complexity of solubility it is difficult to find one molecular descriptor to adequately describe all the solubility processes.

4. CONCLUSION

The two main properties influencing oral absorption are permeability and solubility. In order to establish the relationship of these two properties with oral absorption classification, firstly, a larger dataset was established from different sources. This was made possible through combining Caco-2 and MDCK permeability after comparing a linear relationship between these two cell lines, even for compounds with different absorption mechanisms.

Secondly, using the combined permeability dataset, a permeability threshold for various levels of oral absorption was investigated using CART analysis. Due to the larger number of highly absorbed compounds, misclassification costs were applied and improved the threshold definition statistically. The thresholds obtained from the objective CART analysis are similar

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to some of those in the literature using mainly subjective methods to determine permeability thresholds.

Finally the permeability thresholds were then used to build decision trees with the CART method, incorporating solubility and related parameters, as well as the calculated molecular descriptors to predict oral absorption class. Melting point is not a useful parameter to predict absorption when used stand-alone. However, when melting point is utilised to calculate combined parameters such as predicted (GSE) solubility and melting point-based absorption potential, it yielded high accuracy models compared with experimental solubility. This is due to the possibility of using more data for the training of the models when calculated or more easily accessible experimental parameters are used. Therefore, models built using predicted values of solubility and melting point-based absorption gave rise to better predictive models. Molecular descriptors utilised in the models, such as those describing size, shape, polarizability and hydrogen bonding, can be related to both permeability and solubility and therefore oral absorption. These molecular descriptors were shown to be necessary for oral absorption models to correctly classify the compounds with solubility-limited absorption. The models built in this work are useful for a better mechanistic understanding of the effect of these properties and how they contribute to overall oral absorption.

ASSOCIATED CONTENT

Supporting information I contains the dataset of 932 compounds with HIA%, Caco-2 permeability, MDCK permeability, aqueous solubility, melting point and the references. Supporting information II contains compound lists and information regarding the outliers in Figures 1 and 3 including references. Supporting Information III contains a table comparing the differences in transporter and enzyme expression between the human small intestine, Caco-2 and MDCK cell lines, the significance testing and graphs for the different absorption mechanisms when comparing Caco-2 and MDCK cell lines, all the models (CART decision trees) produced from this work, and finally a list of molecular descriptor utilised in the 12 models presented in this work.

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CAPTIONS (in order of appearance in manuscript)

Table 1. Compound numbers used in the training and validation sets for decision tree analysis

Table 2. Data sets collated from the literature

Figure 1. Linear relationship between Caco-2 and MDCK apparent permeability for 185 compounds

Table 3. Statistical parameters for the linear relationship between MDCK and Caco-2 permeability measured using PRISM

Table 4. The different identified absorption mechanism of the 185 compounds

Table 5. The permeability thresholds selected by CART and HIA class prediction with equal and higher misclassification costs applied to false positives when high HIA defined as higher than 30, 50, 70, 80 and 90%

Figure 2. Permeability thresholds determined by CART analysis with higher misclassification costs applied to false positives for different HIA cut offs of 30%, 50%, 70%, 80% and 90% on %HIA versus permeability plot including areas of outliers (A= low permeability, high oral absorption; B = high permeability, low oral absorption)

Table 6. The results of CART analysis for the best permeability and solubility related trees using permeability threshold for ≥ 80% or < 80% HIA as the first split

1101 **Figure 3.** Model 3 CART permeability and predicted solubility (GSE) model when higher
1102 misclassification costs of two to reduce false positives were applied to low GSE solubility
1103 node

1104 **Figure 4.** Model 7 CART permeability, predicted solubility (GSE) and MPbAP model when
1105 higher misclassification costs of two to reduce false positives were applied to GSE node

1106 **Figure 5.** Model 12 CART permeability and MPbAP model when higher misclassification
1107 costs of two to reduce false positives were applied to permeability node

1108 **Table 7.** Examples of permeability thresholds determined by the literature

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Table 1. Compound numbers used in the training and validation sets for decision tree analysis

Property	Total number of compounds	Training set n	Validation set n
Permeability	433	356	77
Solubility	296	242	54
GSE solubility	315	262	53
Dose number	292	239	53
Melting point	315	262	53
MPbAP	308	257	51

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Table 2. Data sets collated from the literature

Property	n
Human intestinal absorption	932
Caco-2 permeability	386
MDCK permeability	246
Aqueous solubility	482
Dose number	465
Melting point	609

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Table 3. Statistical parameters for the linear relationship between MDCK and Caco-2 permeability measured using PRISM

Datasets	**r^2 (with intercept)**	**r^2 (non-intercept)**	**R_p**	**R_s**
All compounds (185)	0.63	0.60	0.79	0.79
Passive transcellular (83)	0.71	0.69	0.84	0.74
OUTLIERS Removed (9 removed)				
All compounds (176)	0.73	0.72	0.86	0.84
Passive transcellular (81)	0.75	0.75	0.87	0.76

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Table 4. The different identified absorption mechanism of the 185 compounds

Transport route	**Number of compounds**	**Examples**
Passive transcellular (A)	83	sumatriptan, valsartan
Passive paracellular (B)	6	lucifer yellow, mannitol
Efflux (C)	62	vinblastine, saquinavir
Efflux and paracellular (D)	2	famotidine, cimetidine
Influx (E)	15	amoxicillin, tolbutamide
Influx and paracellular (F)	2	soltalol, atenolol
Efflux and influx (G)	14	talinolol, acebutolol
Influx, efflux and paracellular (H)	1	ranitidine

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Table 5. The permeability thresholds selected by CART and HIA class prediction with equal and higher misclassification costs applied to false positives when high HIA defined as higher than 30, 50, 70, 80 and 90%

Model	HIA class determination above or below	Set	Misclassification Costs (FP:FN)	Accuracy (SP X SE)	Sensitivity (SE)	Specificity (SP)	Log Perm Threshold	Perm Threshold (cm/s x10^{-6})
1	30%	t	1:1	0.000	1.000	0.000	-6.11	0.78
		v		0.000	0.986	0.000		
2	50%	t	1:1	0.626	0.905	0.692	-6.02	0.96
		v		0.470	0.939	0.500		
3	70%	t	1:1	0.562	0.910	0.618	-5.91	1.23
		v		0.522	0.948	0.550		
4	80%	t	1:1	0.645	0.745	0.865	-5.15	7.08
		v		0.630	0.741	0.850		
5	90%	t	1:1	0.565	0.785	0.720	-5.08	8.32
		v		0.487	0.762	0.639		
6	30%	t	5:1	0.672	0.874	0.769	-5.98	1.05
		v		**0.800**	**0.914**	**0.875**		
7	50%	t	4:1	0.664	0.803	0.827	-5.64	2.29
		v		0.720	0.864	0.833		
8	70%	t	3:1	0.645	0.745	0.865	-5.15	7.08
		v		0.630	0.741	0.850		
9	80%	t	2.5:1	0.645	0.745	0.865	-5.15	7.08
		v		0.630	0.741	0.850		
10	90%	t	2:1	0.566	0.759	0.745	-5.00	10.0
		v		0.533	0.738	0.722		

t: training set; v: validation set

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Table 6. The results of CART analysis for the best permeability and solubility related trees using permeability threshold for ≥ 80% or < 80% HIA as the first split

Model	Parameter used for second split		Misclassification cost ratios (FP:FN)		Dataset	n	Accuracy (SP x SE)	Sensitivity (SE)	Specificity (SP)
	High permeability compounds	Low permeability compounds	High permeability compounds	Low permeability compounds					
1	Molecular Descriptors[a]	Molecular Descriptors[a]	3:1	6:1	t	356	0.72	0.754	0.955
					v	77	0.519	0.593	0.875
2	Solubility (mg/ml)	Solubility (mg/ml)	2:1	10:1	t	241	0.723	0.823	0.879
					v	54	0.618	0.674	0.917
3	GSE solubility	GSE solubility	2:1	1:1	t	261	0.695	0.891	0.779
					v	53	0.638	0.829	0.769
4	MPbAP	MPbAP	1:1	1:1	t	249	0.753	0.876	0.859
					v	48	0.631	0.757	0.833
5	Solubility (mg/ml)	GSE solubility	2:1	10:1	t	200	0.754	0.820	0.920
					v	40	0.583	0.667	0.875
6	Dose number	MPbAP	2:1	10:1	t	196	0.758	0.791	0.958
					v	40	0.636	0.636	1.000
7	MPbAP	GSE solubility	2:1	1:1	t	256	0.723	0.884	0.818
					v	51	0.667	0.800	0.833
8	MPbAP	Solubility (M)	2:1	1:1	t	197	0.776	0.866	0.896
					v	40	0.697	0.697	1.000
9	Solubility (mg/ml)	Solubility (M)	2:1	10:1	t	241	0.754	0.766	0.985
					v	54	0.533	0.581	0.917
10	GSE solubility	Solubility (M)	2:1	1:1	t	201	0.722	0.881	0.820
					v	40	0.663	0.758	0.875
11	GSE solubility	Molecular Descriptors[a]	2:1	1:1	t	262	0.717	0.887	0.809
					v	53	0.650	0.780	0.833
12	MPbAP	Molecular Descriptors[a]	2:1	1:1	t	257	0.746	0.880	0.848
					v	51	0.688	0.750	0.917

[a] These are the molecular descriptors statistically selected by CART out of all the molecular descriptors and solubility parameters.

FP: false positive; FN: false negative; GSE: General solubility equation; MPbAP: melting point based absorption potential

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Table 7. Examples of permeability thresholds determined by the literature

Study	**Cell line**	**Papp threshold (x 10^{-6} cm/s)**	**Oral absorption class (%)**	**Number of compounds**
Artusson (1991) [37]	Caco-2	>1 ≤ 0.1	100 < 1	20
Yee (1997) [41]	Caco-2	< 1 1-10 >10	0-20 20-70 70-100	35
Bergstrom (2003) [9]	Caco-2	≤ 0.2 ≥ 1.6	≤ 20 ≥ 80	27
Hou (2007) [13]	Caco-2	≥ 6 .0	High (>80)	69
Di (2011) [40]	MDCK II	~ 3	Low/medium (<80) High (>80)	19
Varma (2012) [36]	MDCKII*	≥ 5.0	≥ 80/90	97
Pham-The (2013) [62]	Caco-2	~ 0.7 ≥ 16 .0	< 30 ≥ 85	324

*MDCKII strain (MDCK-LE) cell line with isolated low endogenous efflux transporter expression

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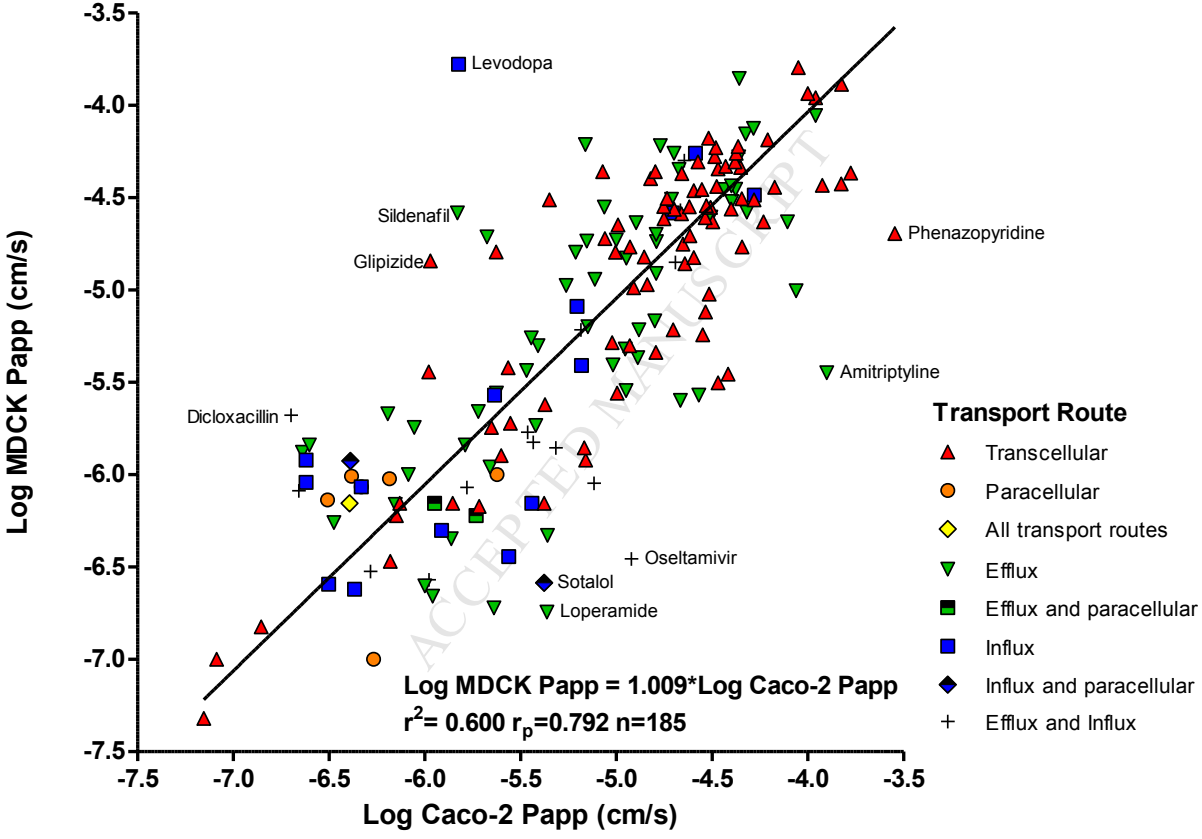

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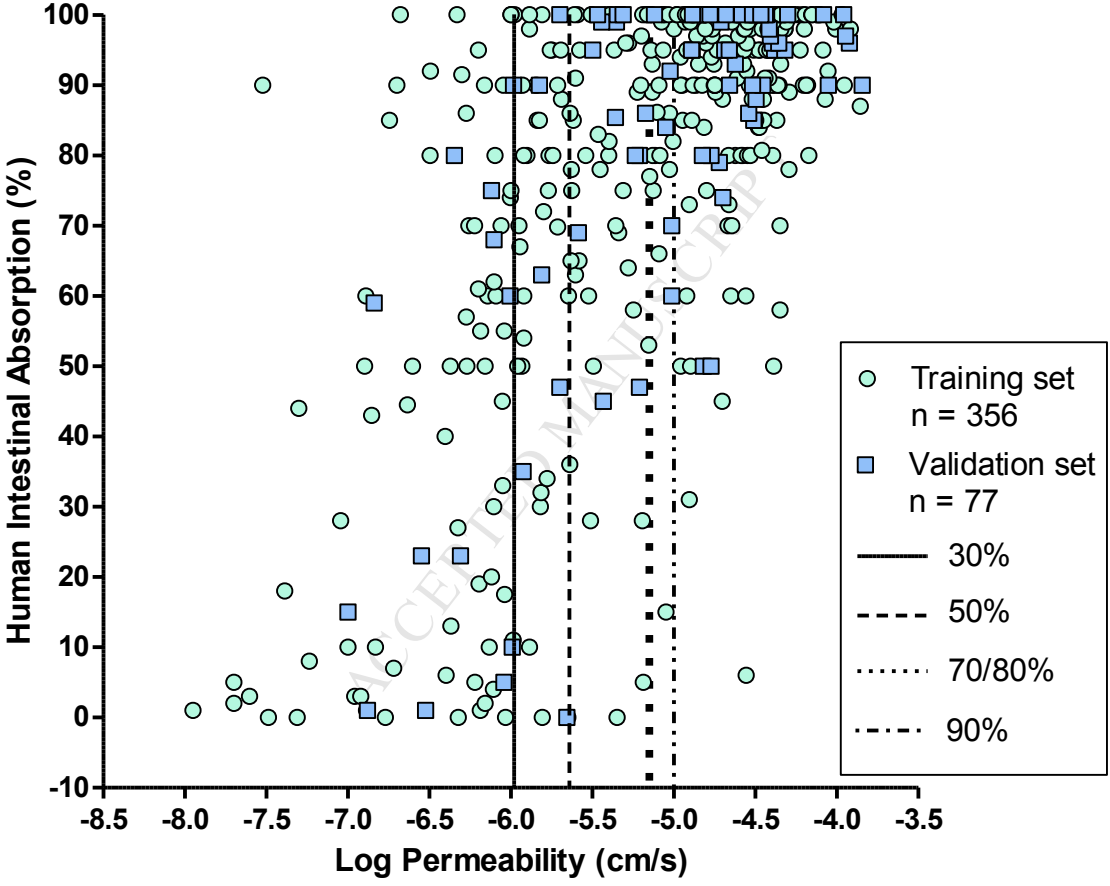

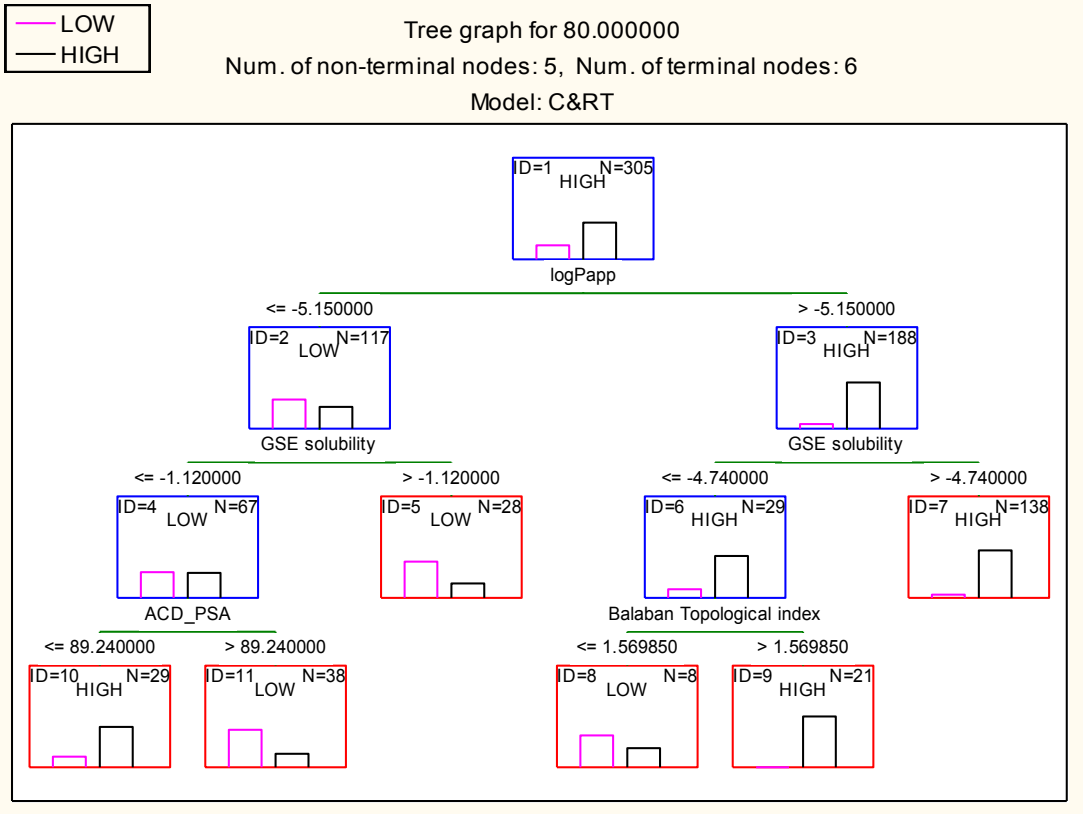
LOW
HIGH
Tree graph for 80.000000
Num. of non-terminal nodes: 5, Num. of terminal nodes: 6
Model: C&RT
ID=1 N=305
HIGH
logPapp
<= -5.150000
> -5.150000
ID=2 N=117
LOW
ID=3 N=188
HIGH
GSE solubility
GSE solubility
<= -1.120000
> -1.120000
<= -4.740000
> -4.740000
ID=4 N=67
LOW
ID=5 N=28
LOW
ID=6 N=29
HIGH
ID=7 N=138
HIGH
ACD_PSA
Balaban Topological index
<= 89.240000
> 89.240000
<= 1.569850
> 1.569850
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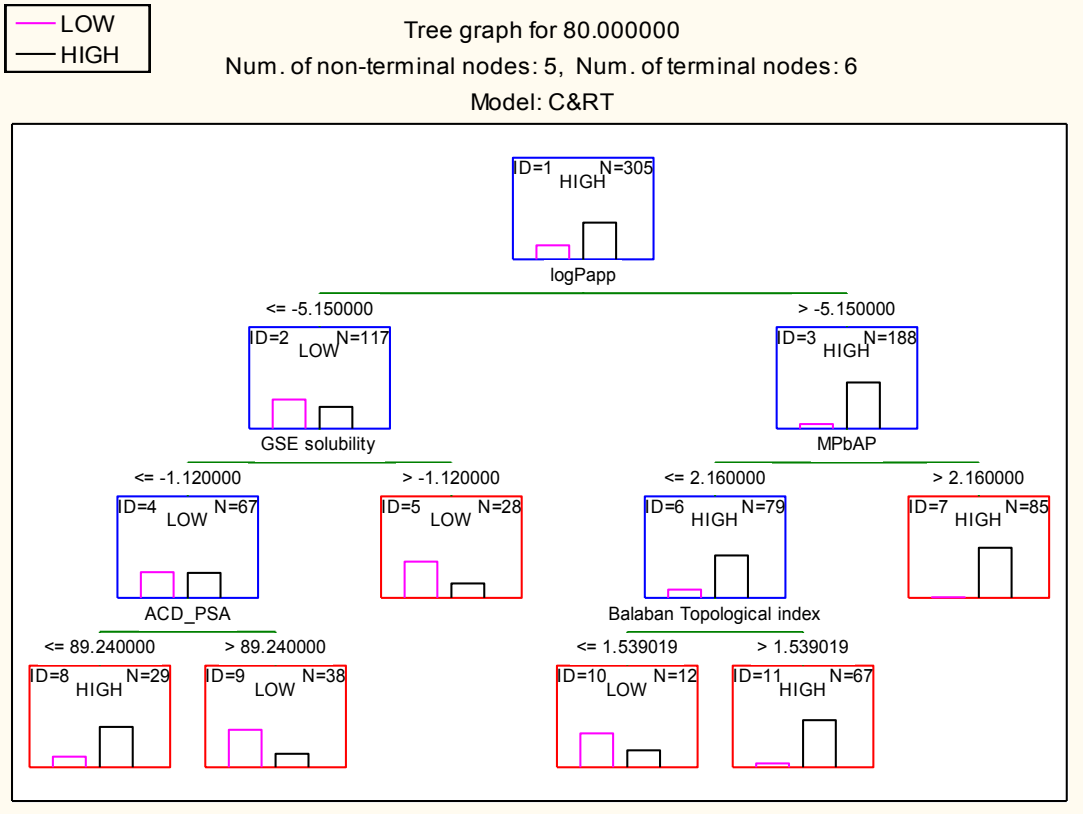
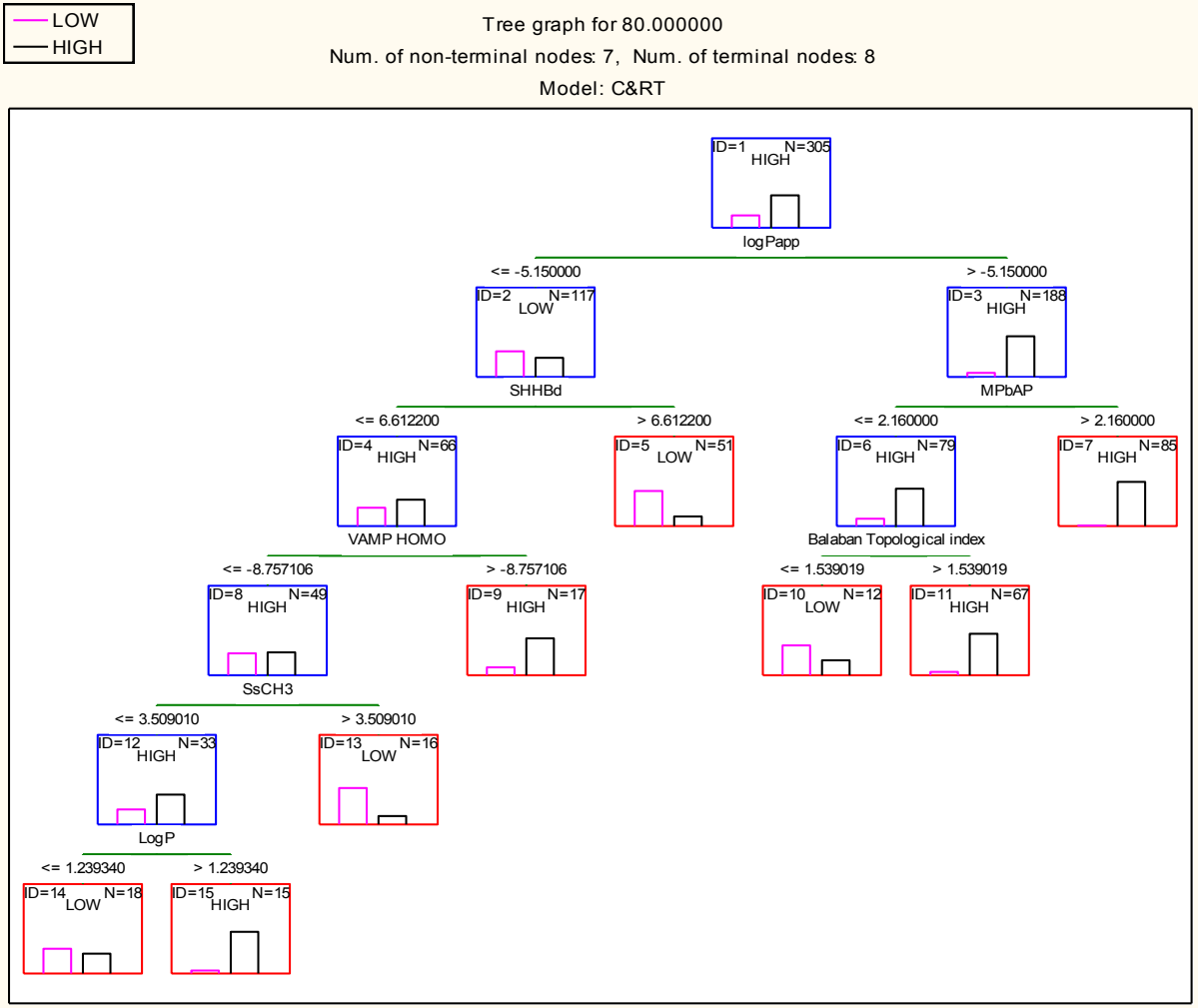
HIGH
ID=11 N=38
LOW
ID=8 N=8
LOW
ID=9 N=21
HIGH


LOW
HIGH
Tree graph for 80.000000
Num. of non-terminal nodes: 5, Num. of terminal nodes: 6
Model: C&RT
ID=1 N=305
HIGH
logPapp
<= -5.150000
> -5.150000
ID=2 N=117
LOW
ID=3 N=188
HIGH
GSE solubility
MPbAP
<= -1.120000
> -1.120000
<= 2.160000
> 2.160000
ID=4 N=67
LOW
ID=5 N=28
LOW
ID=6 N=79
HIGH
ID=7 N=85
HIGH
ACD_PSA
Balaban Topological index
<= 89.240000
> 89.240000
<= 1.539019
> 1.539019
ID=8 N=29
HIGH
ID=9 N=38
LOW
ID=10 N=12
LOW
ID=11 N=67
HIGH


LOW
HIGH
Tree graph for 80.000000
Num. of non-terminal nodes: 7, Num. of terminal nodes: 8
Model: C&RT
ID=1 N=305
HIGH
logPapp
<= -5.150000
> -5.150000
ID=2 N=117
LOW
ID=3 N=188
HIGH
SHHBd
MPbAP
<= 6.612200
> 6.612200
<= 2.160000
> 2.160000
ID=4 N=66
HIGH
ID=5 N=51
LOW
ID=6 N=79
HIGH
ID=7 N=85
HIGH
VAMP HOMO
Balaban Topological index
<= -8.757106
> -8.757106
<= 1.539019
> 1.539019
ID=8 N=49
HIGH
ID=9 N=17
HIGH
ID=10 N=12
LOW
ID=11 N=67
HIGH
SsCH3
<= 3.509010
> 3.509010
ID=12 N=33
HIGH
ID=13 N=16
LOW
LogP
<= 1.239340
> 1.239340
ID=14 N=18
LOW
ID=15 N=15
HIGH

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HIGHLIGHTS

- A large dataset of solubility, permeability and oral absorption was collated
- A permeability threshold was defined to predict oral absorption using decision tree
- Predictive decision trees were developed and the molecular descriptors explained
- Poorly permeable compounds with high solubility show low intestinal absorption
- Poorly water soluble compounds with high or low permeability have high absorption

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SUPPORTING INFORMATION
Complete set of compound names, CAS numbers, pharmacokinetic data, references and comment from authors.

#	Name	# CAS	SMILES	Fraction Absorbed - FA (%)	FA Reference	FA Comments
1	Olsalazine	15722-48-2	Oc1ccc(N=N	8	Cao, D., Wang, J., Zhou, R.	
2	Lincomycin	154-21-2	S(C)C1OC(C(	28	Cao, D., Wang, J., Zhou, R.	
3	Cefuroxime	55268-75-2	S1C2N(C(=O)	44.5	Cao, D., Wang, J., Zhou, R.	
4	Penicillin_V	87-08-1	O=C(O)[C@	59	Cao, D., Wang, J., Zhou, R.	
5	Loperamide_Hydrochloride	53179-11-6	Clc1ccc(cc1)(	76	Therapeutic di	EF
6	Mitoxantrone	65271-80-9	Oc1c2c(C(=C	Poor	Cao, D., Wang, J., Zhou, R.	
7	Bretylium	59-41-6	Brc1ccccc1C	23	Cao, D., Wang, J., Zhou, R.	
8	Amoxicillin	26787-78-0	S1C2N(C(C(C	92	Cao, D., Wang, J., Zhou, R.	
9	Zolmitriptan	139264-17-8	O=C1OC[C@	91.5	Varma, M. V. S., Obach, R.	
10	Acyclovir	59277-89-3	O=C1NC(=Nc	23	Cao, D., Wang, J., Zhou, R.	
11	Sotalol	3930-20-9	S(=O)(=O)(Nc	95	Cao, D., Wang, J., Zhou, R.	
12	Lamivudine	134678-17-4	S1CC(OC1CC	86	Cao, D., Wang, J., Zhou, R.	
13	Sulpiride	15676-16-1	S(=O)(=O)(N)	40	Cao, D., Wang, J., Zhou, R.	
14	Lisinopril	76547-98-3	OC(=O)C1N(C	27	Cao, D., Wang, J., Zhou, R.	
15	Oseltamivir	196618-13-0	O(C(CC)CC)C	75	Cao, D., Wang, J., Zhou, R.	
16	Gabapentin	60142-96-3	OC(=O)C1(CC	74	Stewart BH, Ku	Originally wa
17	Saquinavir	127779-20-8	OC(C(NC(=O)	30	Cao, D., Wang, J., Zhou, R.	
18	Telithromycin	191114-48-4	O1C(CC)C2(C	90	Cao, D., Wang, J., Zhou, R.	
19	Ganciclovir	82410-32-0	O=C2/N=C(\N	4	Cao, D., Wang, J., Zhou, R.	
20	Sulfasalazine	599-79-1	S(=O)(=O)(Nc	13	Cao, D., Wang, J., Zhou, R.	
21	Valsartan	137862-53-4	OC(=O)C(N(C	55	Cao, D., Wang, J., Zhou, R.	
22	Cimetidine	51481-61-9	S(Cc1nc[nH]c	100	Cao, D., Wang	Variable reu
23	Sumatriptan	103628-46-2	S(=O)(=O)(Nc	67	Cao, D., Wang, J., Zhou, R.	
24	Neostigmine	59-99-4	O(C(=O)N(C)	2	Cao, D., Wang, J., Zhou, R.	
25	Ranitidine	66357-35-5	S(Cc1oc(cc1)	57	Cao, D., Wang, J., Zhou, R.	
26	Azithromycin	83905-01-5	O1C(CC)C(O)	60	Varma, M. V. S., Obach, R.	
27	Famotidine	76824-35-6	s1cc(nc1\N=	45	Cao, D., Wang, J., Zhou, R.	
28	Cycloserine	68-41-7	O1NC(=O)C(N	72	Cao, D., Wang, J., Zhou, R.	
29	Tetracycline	60-54-8	C[C@]1(c2cc	80	Cao, D., Wang, J., Zhou, R.	
30	Chlorothiazide	58-94-6	Clc1cc2N=CN	60	Cao, D., Wang, J., Zhou, R.	
31	Lucifer_Yellow	Numerous for di	S(O)(=O)(=O)	0	Cao, D., Wang, J., Zhou, R.	
32	Rosuvastatin	287714-41-4	O=S(=O)(N(c	50	Varma, M. V. S., Obach, R.	
33	Erythromycin	114-07-8	O1C(CC)C(O)	35	Cao, D., Wang, J., Zhou, R.	
34	Baclofen	1134-47-0	Clc1ccc(cc1)(	95	Cao, D., Wang, J., Zhou, R.	
35	Furosemide	54-31-9	Clc1cc(NCc2c	61	Cao, D., Wang, J., Zhou, R.	
36	Talinolol	38649-73-9	O=C(NC1CCC	65	Varma, M. V. S., Obach, R.	
37	Loracarbef	76470-66-1	ClC=1CCC2N	100	Cao, D., Wang, J., Zhou, R.	
38	Hydrochlorothiazide	58-93-5	Clc1cc2NCNS	68	Cao, D., Wang, J., Zhou, R.	
39	Mannitol	69-65-8	OC(C(O)C(O)	19	Cao, D., Wang, J., Zhou, R.	
40	Vinblastine	865-21-4	O=C(OC)[C@	5	Varma, M. V. S., Obach, R.	
41	Terbutaline	23031-25-6	Oc1cc(cc(O)c	63	Cao, D., Wang, J., Zhou, R.	
42	Amisulpride	71675-85-9	O=S(=O)(c1c	100	Varma, M. V. S., Obach, R.	
43	Atenolol	29122-68-7	O(CC(O)CNC	50	Cao, D., Wang, J., Zhou, R.	
44	Methyldopa	555-30-6	Oc1cc(ccc1C	50	Cao, D., Wang, J., Zhou, R.	
45	Carvedilol	72956-09-3	O(CCNCC(OC	80	Cao, D., Wang, J., Zhou, R.	
46	Practolol	6673-35-4	OC(CNC(C)C)	95	Cao, D., Wang, J., Zhou, R.	
47	Methotrexate	59-05-2	O=C(O)[C@	70	Varma, M. V. S., Obach, R.	
48	Ciprofloxacin	85721-33-1	Fc1cc2c(nc1N	69	Cao, D., Wang, J., Zhou, R.	
49	Netivudine	84558-93-0	O1C(CO)C(O	28	Cao, D., Wang, J., Zhou, R.	
50	Doxorubicin	23214-92-8	O1C(C)C(O)C	5	Cao, D., Wang, J., Zhou, R.	

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51	Nadolol	42200-33-9	O(CC(O)CNC	32	Cao, D., Wang, J., Zhou, R. e
52	Digoxin	20830-75-5	O1C(C)C(OC2	78	Cao, D., Wang, J., Zhou, R. e
53	Acebutolol	37517-30-9	O(CC(O)CNC	85	Cao, D., Wang, J., Zhou, R. e
54	Losartan	114798-26-4	Clc1nc(n(Cc2	80	Cao, D., Wang, J., Zhou, R. e
55	Doxycycline	564-25-0	O=C3/C(=C(/	100	Varma, M. V. S., Obach, R. S
56	Domperidone	57808-66-9	Clc1cc2NC(=	95	Cao, D., Wang, J., Zhou, R. e
57	Sertraline hydrochloride	79559-97-0	Clc1ccc(cc1C	86	http://www.a EU/EF
58	Dicloxacillin	3116-76-5	O=C(O)[C@(	100	Varma, M. V. S., Obach, R. S
59	Etoposide	33419-42-0	O1C2C(OC(C	50	Cao, D., Wang, J., Zhou, R. e
60	Acrivastine	87848-99-5	OC(=O)\C=C\	88	Cao, D., Wang, J., Zhou, R. e
61	Disopyramide	3737-09-5	O=C(N)C(CCI	95	Cao, D., Wang, J., Zhou, R. e
62	Amprenavir	161814-49-9	O=C(O[C@H	89	Sadler BM, Chi Extensively m
63	Enalapril	75847-73-3	OC(=O)C1N((	63	Cao, D., Wang, J., Zhou, R. e
64	Levofloxacin	100986-85-4	C[C@H]1CO(	100	Varma, M. V. S., Obach, R. S
65	Cetirizine	83881-51-0	Clc1ccc(cc1)(	100	Cao, D., Wang, J., Zhou, R. e
66	Minoxidil	38304-91-5	[O-][n+]1ccc	96	Cao, D., Wang, J., Zhou, R. e
67	Dipyridamole	58-32-2	OCCN(CCO)c	58	Cao, D., Wang, J., Zhou, R. e
68	Chloramphenicol	56-75-7	ClC(Cl)C(=O)I	90	Cao, D., Wang, J., Zhou, R. e
69	Flecainide	54143-55-4	FC(F)(F)COc1	81	Cao, D., Wang, J., Zhou, R. e
70	Amitriptyline	50-48-6	N(CC\C=C/1\	95	Cao, D., Wang, J., Zhou, R. e
71	Bosentan	147536-97-8	CC(C)(C)c1cc	69.8	Weber, C, Gas EU/EF
72	Nelfinavir	159989-64-7	O=C(c1cccc((	78	http://www.accessdata.fda
73	Amiloride	2016-88-8	Clc1nc(C(=O)	50	Cao, D., Wang, J., Zhou, R. e
74	Cephalexin	15686-71-2	S1C2N(C(=O)	96	Cao, D., Wang, J., Zhou, R. e
75	Crizotinib	877399-52-5	C[C@H](c1c(	47	http://www.a BA/EU/EF
76	Ketoconazole	65277-42-1	Clc1cc(Cl)ccc	75	Cao, D., Wang, J., Zhou, R. e
77	Ofloxacin	82419-36-1	Fc1cc2c3N(C	100	Cao, D., Wang, J., Zhou, R. e
78	Chloroquine	54-05-7	Clc1cc2nccc(	100	Cao, D., Wang, J., Zhou, R. e
79	Ritonavir	155213-67-5	CC(C)c4nc(CI	70	Varma, M. V. S., Obach, R. S
80	Fluoxetine	54910-89-3	FC(F)(F)c1cc(	80	Cao, D., Wang, J., Zhou, R. e
81	Rifabutin	72559-06-9	CC(C)CN1CC(	53	Varma, M. V. S., Obach, R. S
82	Prednisolone	50-24-8	OC1(CCC2C3	99	Cao, D., Wang, J., Zhou, R. e
83	Norethindrone	68-22-4	OC1(CCC2C3	100	Cao, D., Wang, J., Zhou, R. e
84	Zidovudine	30516-87-1	O1C(CO)C(N=	97	Cao, D., Wang, J., Zhou, R. e
85	Tacrolimus	104987-11-3	O=C3C(=O)N	15	Varma, M. V. S., Obach, R. S
86	Atropine	51-55-8	O(C(=O)C(CC	94	Cao, D., Wang, J., Zhou, R. e
87	Ethinyl_Estradiol	57-63-6	OC1(CCC2C3	100	Cao, D., Wang, J., Zhou, R. e
88	Clozapine	5786-21-0	Clc1cc2N=C(	100	Cao, D., Wang, J., Zhou, R. e
89	Cisapride	81098-60-4	Clc1cc(C(=O)	100	Cao, D., Wang, J., Zhou, R. e
90	Ascorbic_Acid	50-81-7	O1C(C(O)CO	100	Cao, D., Wang, J., Zhou, R. e
91	Fluconazole	86386-73-4	Fc1cc(F)ccc1	94	Cao, D., Wang, J., Zhou, R. e
92	Trimethoprim	738-70-5	O(C)c1c(OC)(	98	Cao, D., Wang BA
93	Ziprasidone	146939-27-7	Clc1cc2NC(=	90	Varma, M. V. S., Obach, R. S
94	Terfenadine	50679-08-8	OC(C1CCN(C	100	Cao, D., Wang, J., Zhou, R. e
95	Lovastatin	75330-75-5	O=C(O[C@@	31	Varma, M. V. S., Obach, R. S
96	Prazosin	19216-56-9	o1cccc1C(=C	86	Cao, D., Wang, J., Zhou, R. e
97	Haloperidol	52-86-8	Clc1cc(ccc1)(	100	Cao, D., Wang, J., Zhou, R. e
98	Felodipine	72509-76-3	Clc1c(cccc1C	90	Cao, D., Wang, J., Zhou, R. e
99	Quinidine	56-54-2	O(C)c1cc2c(n	80	Cao, D., Wang, J., Zhou, R. e
100	Glipizide	29094-61-9	S(=O)(=O)(N(	100	Cao, D., Wang, J., Zhou, R. e
101	Prednisone	53-03-2	O=C(CO)[C@	95	Cao, D., Wang, J., Zhou, R. e
102	Fluvastatin	93957-54-1	Fc1ccc(cc1)-(	100	Cao, D., Wang, J., Zhou, R. e
103	Citalopram	59729-33-8	Fc1ccc(cc1)C	100	Cao, D., Wang, J., Zhou, R. e
104	Methylprednisolone	83-43-2	OC1(CCC2C3	82	Cao, D., Wang, J., Zhou, R. e
105	Propafenone	54063-53-5	O(CC(O)CNC(	95	Cao, D., Wang, J., Zhou, R. e
106	Hydroxyzine	68-88-2	Clc1ccc(cc1)(	80	Cao, D., Wang BA
107	Scopolamine	51-34-3	O1C2C3N(C(	93	Cao, D., Wang, J., Zhou, R. e
108	Theophylline	58-55-9	O=C1N(C)C(=	100	Cao, D., Wang, J., Zhou, R. e
109	Metoclopramide	364-62-5	Clc1cc(C(=O)	88	Cao, D., Wang, J., Zhou, R. e

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110	Imipramine	50-49-7	N(CCCN1c2c	98	Cao, D., Wang, J., Zhou, R. e
111	Astemizole	68844-77-9	Fc1ccc(cc1)C	100	Cao, D., Wang, J., Zhou, R. e
112	Morphine	57-27-2	O1C2C34C(C	90	Cao, D., Wang, J., Zhou, R. e
113	Labetalol	36894-69-6	Oc1ccc(cc1C	95	Cao, D., Wang, J., Zhou, R. e
114	Bromocriptine	25614-03-3	BrC1Nc2c3C	28	Cao, D., Wang, J., Zhou, R. e
115	Trazodone	19794-93-5	Clc1cc(N2CC	100	Cao, D., Wang, J., Zhou, R. e
116	Dexamethasone	50-02-2	FC12C(C3CC	90	Cao, D., Wang, J., Zhou, R. e
117	Phenazopyridine	94-78-0	n1c(N)c(N=N	90	Cao, D., Wang, J., Zhou, R. e
118	Ephedrine	50906-05-3	OC(c1ccccc1	97	Sever, P. S., Dr EU
119	Risperidone	106266-06-2	Fc1cc2onc(c1	97	Cao, D., Wang, J., Zhou, R. e
120	Zolpidem	82626-48-0	O=C(N(CCC)C	95	Cao, D., Wang, J., Zhou, R. e
121	Diclofenac	15307-86-5	Clc1cc(Cl)ccc	100	Cao, D., Wang, J., Zhou, R. e
122	Lansoprazole	103577-45-3	S(=O)(Cc1nc(	85	Cao, D., Wang, J., Zhou, R. e
123	Metoprolol	37350-58-6	O(CC(O)CNC	96	Cao, D., Wang, J., Zhou, R. e
124	Lorazepam	846-49-1	Clc1ccccc1C1	95	Cao, D., Wang, J., Zhou, R. e
125	Mebendazole	31431-39-7	O(C(=O)Nc1[	6	Cao, D., Wang, J., Zhou, R. e
126	Methadone	76-99-3	O=C(C(CC(N(	80	Cao, D., Wang, J., Zhou, R. e
127	Ketoprofen	22071-15-4	OC(=O)C(C)c	95	Cao, D., Wang, J., Zhou, R. e
128	Sildenafil	139755-83-2	O=S(=O)(N1C	92	Varma, M. V. S., Obach, R. S
129	Loratadine	79794-75-5	Clc1cc2c(cc1	90	Cao, D., Wang, J., Zhou, R. e
130	Glyburide	10238-21-8	Clc1cc(C(=O)	100	Cao, D., Wang, J., Zhou, R. e
131	Flurbiprofen	5104-49-4	Fc1cc(ccc1)-	95	Cao, D., Wang, J., Zhou, R. e
132	Bromazepam	1812-30-2	Brc1cc2c(NC	84	Cao, D., Wang, J., Zhou, R. e
133	Naproxen	22204-53-1	O(C)c1cc2c(c	100	Cao, D., Wang, J., Zhou, R. e
134	Chlorpromazine	50-53-3	Clc1cc2N(c3	98	Cao, D., Wang, J., Zhou, R. e
135	Repaglinide	135062-02-1	O(CC)c1cc(cc	100	Cao, D., Wang, J., Zhou, R. e
136	Oxycodone	76-42-6	O1C2C34CCN	60	Cao, D., Wang, J., Zhou, R. e
137	Phenytoin	57-41-0	O=C1NNC(=C	90	Cao, D., Wang, J., Zhou, R. e
138	Lopinavir	192725-17-0	O=C(N[C@@	80.7	Kumar GN, Jay EU/EF
139	Pheniramine	86-21-5	n1ccccc1C(C	99	Cao, D., Wang, J., Zhou, R. e
140	Oxprenolol	6452-71-7	O(CC(O)CNC	95	Cao, D., Wang, J., Zhou, R. e
141	Hydrocortisone	50-23-7	OC1(CCC2C3	91	Cao, D., Wang, J., Zhou, R. e
142	Caffeine	58-08-2	O=C1N(C)C(=	100	Cao, D., Wang, J., Zhou, R. e
143	Diflunisal	22494-42-4	Fc1cc(F)ccc1	100	Cao, D., Wang, J., Zhou, R. e
144	Tolbutamide	64-77-7	S(=O)(=O)(NC	90	Cao, D., Wang, J., Zhou, R. e
145	Buspirone	36505-84-7	O=C1N(CCCC	100	Cao, D., Wang, J., Zhou, R. e
146	Triazolam	28911-01-5	Clc1ccccc1C1	85	Cao, D., Wang, J., Zhou, R. e
147	Acetaminophen	103-90-2	Oc1ccc(NC(=	85	Cao, D., Wang, J., Zhou, R. e
148	Ibuprofen	15687-27-1	OC(=O)C(C)c	98	Cao, D., Wang, J., Zhou, R. e
149	Diazepam	439-14-5	Clc1cc2c(N(C	99	Cao, D., Wang, J., Zhou, R. e
150	Oxaprozin	21256-18-8	o1c(c(nc1CC	98	Cao, D., Wang, J., Zhou, R. e
151	Diltiazem	33286-22-5	OC1CC2=CC(	91	Cao, D., Wang, J., Zhou, R. e
152	Alprazolam	28981-97-7	Clc1cc2c(-n3	90	Cao, D., Wang, J., Zhou, R. e
153	Alfentanil	71195-58-9	O=C1N(\N=N	100	Varma, M. V. S., Obach, R. S
154	Naltrexone	16590-41-3	O1C2C34CCN	95	Cao, D., Wang, J., Zhou, R. e
155	Amantadine	768-94-5	NC12CC3CC(	90	Cao, D., Wang, J., Zhou, R. e
156	Promethazine	60-87-7	S1c2c(N(c3c1	88	Cao, D., Wang, J., Zhou, R. e
157	Chlorpheniramine	132-22-9	Clc1ccc(N(CC	80	Cao, D., Wang, J., Zhou, R. e
158	Tacrine	321-64-2	n1c2c(CCCC2	95	Cao, D., Wang, J., Zhou, R. e
159	Propranolol	525-66-6	OC(C(NC(C)C	95	Cao, D., Wang, J., Zhou, R. e
160	Warfarin	81-81-2	O1c2c(cccc2	97	Cao, D., Wang, J., Zhou, R. e
161	Alprenolol	13655-52-2	O(CC(O)CNC	93	Cao, D., Wang, J., Zhou, R. e
162	Indomethacin	53-86-1	O(C)c1cc2c(n	100	Cao, D., Wang, J., Zhou, R. e
163	Carbamazepine	298-46-4	O=C(N)N1c2	100	Cao, D., Wang, J., Zhou, R. e
164	Naloxone	465-65-6	O1C2C34CCN	91	Cao, D., Wang, J., Zhou, R. e
165	Verapamil	52-53-9	O(C)c1cc(ccc	95	Cao, D., Wang, J., Zhou, R. e
166	Midazolam	59467-70-8	Clc1cc2c(-n3	100	Cao, D., Wang, J., Zhou, R. e
167	Clonidine	4205-90-7	Clc1cccc(Cl)c	95	Cao, D., Wang, J., Zhou, R. e
168	Timolol	26839-75-8	s1nc(N2CCO	95	Cao, D., Wang, J., Zhou, R. e

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169	Desipramine	50-47-5	N(CCCN1c2c	98	Cao, D., Wang, J., Zhou, R. e
170	Antipyrine	60-80-0	O=C1N(N(C)(	98	Cao, D., Wang, J., Zhou, R. e
171	Pindolol	13523-86-9	O(CC(O)CNC	90	Cao, D., Wang, J., Zhou, R. e
172	Guanabenz	5051-62-7	Clc1cccc(Cl)c	78	Cao, D., Wang, J., Zhou, R. e
173	Nitrendipine	39562-70-4	O(C(=O)C=1(	88	Cao, D., Wang, J., Zhou, R. e
174	Nicardipine	55985-32-5	O(C(=O)c1c((	95	Cao, D., Wang, J., Zhou, R. e
175	Lidocaine	137-58-6	O=C(Nc1c(cc	98	Cao, D., Wang, J., Zhou, R. e
176	Piroxicam	36322-90-4	S1(=O)(=O)N	100	Cao, D., Wang, J., Zhou, R. e
177	Tamoxifen	10540-29-1	O(CCN(C)C)c	100	Cao, D., Wang, J., Zhou, R. e
178	Nifedipine	21829-25-4	O(C(=O)C)C=	90	Cao, D., Wang, J., Zhou, R. e
179	Lamotrigine	84057-84-1	Clc1c(cccc1C	98	Cao, D., Wang, J., Zhou, R. e
180	Ondansetron	99614-02-5	O=C1c2c(n(c	100	Cao, D., Wang, J., Zhou, R. e
181	Testosterone	58-22-0	OC1CCC2C3(	100	Cao, D., Wang, J., Zhou, R. e
182	Bupropion	34841-39-9	Clc1ccc(cc1)(	87	Cao, D., Wang, J., Zhou, R. e
183	Corticosterone	50-22-6	OC1C2C(C3C	100	Cao, D., Wang, J., Zhou, R. e
184	Progesterone	57-83-0	O=C1CCC2(C	96	Cao, D., Wang, J., Zhou, R. e
185	Levodopa	59-92-7	Oc1cc(ccc1C	86	Cao, D., Wang, J., Zhou, R. e
186	Alendronic_Acid	66376-36-1	P(O)(O)(=O)(	1	Cao, D., Wang, J., Zhou, R. e
187	Deferoxamine	70-51-9	CC(=O)N(CC(	2	Cao, D., Wang, J., Zhou, R. e
188	HBED	35998-29-9	O=C(O)CN(C(	5	Gunturi, S.B. and Narayana
189	Clodronate	10596-23-3	ClC(Cl)(P(O)(	3	Cao, D., Wang, J., Zhou, R. e
190	Folinic_Acid	1492-18-8	O=C1N=C(N(	90	Cao, D., Wang, J., Zhou, R. e
191	Piperacillin	61477-96-1	O=C(O)[C@@	0	Cao, D., Wang, J., Zhou, R. e
192	Foscarnet	63585-09-1	P(O)(O)(=O)(	18	Cao, D., Wang, J., Zhou, R. e
193	Raffinose	512-69-6	O1C(OC2OC(	0	Cao, D., Wang, J., Zhou, R. e
194	Lercanidipine	100427-26-7	[O-][N+](=O)	44	Barchielli, M.; BA/EU
195	Cefmetazole	56796-20-4	S1C2N(C(=O)	10	Cao, D., Wang, J., Zhou, R. e
196	Melagatran	192939-46-1	O=C(NCc1cc(	15	Varma, M. V. S., Obach, R. S
197	Ouabain	630-60-4	O1C(C)C(O)C	3	Cao, D., Wang, J., Zhou, R. e
198	Amphotericin_B	1397-89-3	O1C(C)C(O)C	3	Cao, D., Wang, J., Zhou, R. e
199	Benazepril	86541-75-5	O=C1N(c2c((	50	Cao, D., Wang, J., Zhou, R. e
200	Fenoterol	13392-18-2	Oc1cc(cc(O)(	60	Cao, D., Wang, J., Zhou, R. e
201	Cromolyn	16110-51-3	O=C(O)C=4O	1	Cao, D., Wang, J., Zhou, R. e
202	Ceftriaxone	73384-59-5	s1cc(nc1N)/(	1	Cao, D., Wang, J., Zhou, R. e
203	Metaproterenol	586-06-1	Oc1cc(cc(O)(	43	Cao, D., Wang, J., Zhou, R. e
204	Trospium	10405-02-4	O(C(=O)C(O)	10	Cao, D., Wang, J., Zhou, R. e
205	Vidarabine	24356-66-9	n2c1c(ncnc1	0	Cao, D., Wang, J., Zhou, R. e
206	Ribavirin	36791-04-5	c1nc(nn1[C@	85	Cao, D., Wang, J., Zhou, R. e
207	Xamoterol	81801-12-9	O=C(NCCNC(	7	Cao, D., Wang, J., Zhou, R. e
208	Diphenoxylate	915-30-0	N#CC(c1cccc	90	Cao, D., Wang, BA
209	Acetazolamide	59-66-5	s1c(nnc1S(=(	100	Cao, D., Wang, EU/BA
210	Didanosine	69655-05-6	O=C3/N=C\N	50	Varma, M. V. S., Obach, R. S
211	Lactulose	4618-18-2	O1C(O)(CO)(	1	Cao, D., Wang, J., Zhou, R. e
212	Mesalamine	89-57-6	Oc1ccc(N)cc	80	http://www.a Hou 2012 st
213	Tiludronic_Acid	89987-06-4	Clc1ccc(cc1)(	6	Cao, D., Wang, J., Zhou, R. e
214	Oseltamivir_Acid	187227-45-8	O=C(N[C@H]	80	Varma, M. V. S., Obach, R. S
215	Pimozide	2062-78-4	Fc1ccc(cc1)C	70	Cao, D., Wang, J., Zhou, R. e
216	Aztreonam	78110-38-0	s1cc(nc1N)/(	1	Cao, D., Wang, J., Zhou, R. e
217	Floxuridine	50-91-9	FC=1C(=O)N(	90	Cao, D., Wang, BA
218	Cefatrizine	51627-14-6	S1C2N(C(=O)	75	Cao, D., Wang, J., Zhou, R. e
219	Pirenzepine_Hydrochloride	28797-61-7	O=C3c1cccc(	>20	Therapeutic dı EU/EF
220	Ampicillin	69-53-4	S1C2N(C(C(C	62	Cao, D., Wang, J., Zhou, R. e
221	Ivermectin	70288-86-7	O1C(C)C(O)C	60	Cao, D., Wang, J., Zhou, R. e
222	Ceftibuten	97519-39-6	O=C2N1/C(=	70	Lin, C., Lim, J., EU
223	Cyclosporine_A	59865-13-3	O=C1N(C)C((	33	Cao, D., Wang, J., Zhou, R. e
224	Tranexamic_Acid	1197-18-8	OC(=O)C1CC	55	Cao, D., Wang, J., Zhou, R. e
225	Methylscopolamine	13265-10-6	O=C(OC1C[C	17.5	Cao, D., Wang, J., Zhou, R. e
226	Pentamidine	100-33-4	O(CCCCCOc1	0	Cao, D., Wang, J., Zhou, R. e
227	Gemcitabine	95058-81-4	c1cn(c(=O)n(	100	Cao, D., Wang, J., Zhou, R. e

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228	Maraviroc	376348-65-1	Cc5nnc(n5[C	75	Walker DK, Ab EU/EF
229	Acamprosate	77337-76-9	S(O)(=O)(=O)	11	Cao, D., Wang, J., Zhou, R.
230	Ginkgolide_B	15291-77-7	CC1C(=O)OC	90	Varma, M. V. S., Obach, R.
231	Entacapone	130929-57-6	[O-][N+](=O)	50	Varma, M. V. S., Obach, R.
232	Creatinine	60-27-5	CN1CC(=O)N	70	Tavelin, S., Taipalensuu, J.,
233	Pregabalin	148553-50-8	O=C(O)C[C@	90	Cao, D., Wang, J., Zhou, R.
234	Atazanavir sulfate	198904-31-3	O=S(=O)(O)C	80	http://www.a EU/EF
235	Cefixime	79350-37-1	s1c(cnc1N)/(	60	Cao, D., Wang, J., Zhou, R.
236	Metformin	657-24-9	N(C(NC(N)=N	54	Cao, D., Wang, J., Zhou, R.
237	Bendroflumethiazide	73-48-3	S(=O)(=O)(N)	100	Cao, D., Wang, J., Zhou, R.
238	Enalaprilat	76420-72-9	O(C(=O)C(NC	10	Cao, D., Wang, J., Zhou, R.
239	Sulfamethizole	144-82-1	s1c(nnc1NS(	85	Cao, D., Wang, J., Zhou, R.
240	Vildagliptin	274901-16-5	N#C[C@H]4I	85	He YL., Clin Ph BA
241	Cefaclor	53994-73-3	O=C2N1/C(=	90	Cao, D., Wang BA
242	Penicillin G	61-33-6	S1C2N(C(C(C	30	Zhao YH, Le J, Abraham MH
243	Cefotaxime	63527-52-6	s1cc(nc1N)/(	0	Cao, D., Wang, J., Zhou, R.
244	Pravastatin	81093-37-0	O(C(=O)C(CC	34	Cao, D., Wang, J., Zhou, R.
245	Folic_Acid	59-30-3	O=C1NC(=Nc	75	Cao, D., Wang, J., Zhou, R.
246	Octreotide	83150-76-9	C[C@@H](O	Poor	Therapeutic drugs, 2ed (19
247	Amlodipine	88150-42-9	Clc1ccccc1C2	95	Varma, M. V. S., Obach, R.
248	Terbinafine	91161-71-6	N(Cc1c2c(cc	80	Cao, D., Wang, J., Zhou, R.
249	Vardenafil	224785-90-4	CCCc1nc(c2n	90	Varma, M. V. S., Obach, R.
250	Cymarin	508-77-0	O1C(C)C(O)C	47	Cao, D., Wang, J., Zhou, R.
251	Cephradine	38821-53-3	S1C2N(C(=O)	95	Cao, D., Wang, J., Zhou, R.
252	Ceftazidime	72558-82-8	s1cc(nc1N)/(	0	Cao, D., Wang, J., Zhou, R.
253	Cefamandole_Nafate	34444-01-4	O=C2N1/C(=	0	Yalkowsky, S.H., Johnson, J
254	Raloxifene	84449-90-1	O=C(c1c3ccc	60	Cao, D., Wang, J., Zhou, R.
255	Valaciclovir	124832-26-4	O=C(OCCOC	36	Fagerholm, U., REV
256	Formoterol_Fumarate	73573-87-2	O=CNc1cc(cc	65	Therapeutic dr EU/EF
257	Norfloxacin	70458-96-7	Fc1cc2c(N(C3	75	Cao, D., Wang, J., Zhou, R.
258	Isoxicam	34552-84-6	S1(=O)(=O)c2	100	Cao, D., Wang, J., Zhou, R.
259	Zomepirac	33369-31-2	Clc1ccc(cc1)(	100	Cao, D., Wang, J., Zhou, R.
260	Aspirin	50-78-2	O(C(=O)C)c1	91	Cao, D., Wang, J., Zhou, R.
261	Levothyroxine_Sodium	51-48-9	[O-]C(=O)[C@	60	http://www.a variable abs
262	Cefazolin	25953-19-9	O=C2N1/C(=	100	Varma, M. V. S., Obach, R.
263	Clarithromycin	81103-11-9	CN(C)[C@H]1	100	Varma, M. V. S., Obach, R.
264	Lomefloxacin	98079-51-7	Fc1c2N(C=C(	99	Cao, D., Wang, J., Zhou, R.
265	Abiraterone_Acetate	154229-19-3	O=C(O[C@@	>45	Acharya M, Gc EF
266	Rifampin	13292-46-1	O1c2c3c4c(c	80	Cao, D., Wang, J., Zhou, R.
267	Sorivudine	77181-69-2	Br\C=C\C1CN	82	Cao, D., Wang, J., Zhou, R.
268	Norgestrel	6533-00-2	OC1(CCC2C3	100	Cao, D., Wang, J., Zhou, R.
269	Ketorolac	74103-06-3	OC(=O)C1CC	95	Cao, D., Wang, J., Zhou, R.
270	Levocetirizine dihydrochloride	130018-77-8	Clc1ccc(cc1)[	85.4	http://www.a EU
271	Cephalothin	153-61-7	O=C2N1/C(=	0	Cao, D., Wang, J., Zhou, R.
272	Stavudine	3056-17-5	O1C(C=CC1N	100	Cao, D., Wang, J., Zhou, R.
273	Mibefradil	116644-53-2	Fc1cc2c(cc1)	69	Cao, D., Wang, J., Zhou, R.
274	Rilpivirine	500287-72-9	N#C\C=C\c1c	75	James C, Prein EU/EF/REV
275	Metolazone	17560-51-9	Clc1cc2NC(N	64	Cao, D., Wang REV
276	Cinacalcet	226256-56-0	FC(F)(F)c1cc	80	Kumar GN, Spi EU/EF
277	Enoxacin	74011-58-8	Fc1c(nc2c(c1	89	Chang T, Black BA
278	Sulindac	38194-50-2	S(=O)(C)c1cc	90	Cao, D., Wang, J., Zhou, R.
279	Cerivastatin	145599-86-6	O=C(O)C[C@	100	Varma, M. V. S., Obach, R.
280	Albendazole	54965-21-8	O=C(OC)Nc2	5	Cao, D., Wang, J., Zhou, R.
281	UK-294,315		O=C(N1CCCN	86	Harrison A, Be EF
282	Linezolid	165800-03-3	Fc1cc(N2CC(	100	Cao, D., Wang, J., Zhou, R.
283	Dexloxiglumide	119817-90-2	Clc1ccc(C(=C	95	Varma, M. V. S., Obach, R.
284	Sulfadiazine	68-35-9	O=S(=O)(Nc1	93	Cao, D., Wang, J., Zhou, R.
285	Methoxyamphetamine	17862-85-0	O(C)c1cc(ccc	80	Cao, D., Wang, J., Zhou, R.
286	Paricalcitol	131918-61-1	O[C@@H]3C	86.1	Varma, M. V. S., Obach, R.

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287	Rivaroxaban	366789-02-8	c1cc(ccc1N2	66	Weinz C, Schw EU/EF
288	Terazosin	63590-64-7	O1CCCC1C(=	90	Cao, D., Wang, J., Zhou, R. e
289	Riboflavin	83-88-5	O=C1NC(=O)	80	Cao, D., Wang, J., Zhou, R. e
290	Tolmetin	26171-23-3	OC(=O)Cc1n	99	Cao, D., Wang, J., Zhou, R. e
291	Cefadroxil	66592-87-8	S1C2N(C(=O	100	Cao, D., Wang, J., Zhou, R. e
292	Milnacipran	92623-85-3	O=C(N(CC)C(	84	Cao, D., Wang, BA
293	Budesonide	51333-22-3	O1C2(C(OC1	100	Cao, D., Wang, J., Zhou, R. e
294	Boceprevir	394730-60-0	O=C(N3[C@H	92	Kiser, J.J., Burt EF
295	Olopatadine_Hydrochloride	140462-76-6	O=C(O)Cc2c(	70	Tsunoo,M., M EU/REV
296	Phenylbutazone	50-33-9	O=C1C(N(N(	98	Cao, D., Wang, J., Zhou, R. e
297	Orphenadrine	83-98-7	O(C(c1ccccc1	100	Cao, D., Wang, J., Zhou, R. e
298	Tegaserod	189188-57-6	CCCCCNC(=N	50	Varma, M. V. S., Obach, R. S
299	Dapsone	80-08-0	S(=O)(=O)(c1	90	Cao, D., Wang, J., Zhou, R. e
300	Fenoprofen	31879-05-7	O(c1cc(ccc1)	85	Cao, D., Wang, J., Zhou, R. e
301	Irbesartan	138402-11-6	O=C1N(Cc2c	100	Cao, D., Wang, J., Zhou, R. e
302	Gemifloxacin	175463-14-6	Fc2c(nc1N(/(	60	Allen, A., Bird, RA/EU/EF
303	Sulfisoxazole	127-69-5	s1nc(C)c(C)c1	95	Cao, D., Wang, J., Zhou, R. e
304	Spironolactone	52-01-7	S(C(=O)C)C1(	73	Cao, D., Wang, J., Zhou, R. e
305	Tiacrilast	78299-53-3	S(C)c1cc2c(N	99	Cao, D., Wang, J., Zhou, R. e
306	Clopidogrel bisulfate	90055-48-4	COC(=O)[C@	>50	http://www.a EU-EF
307	Dolasetron	115956-13-3	O(C(=O)c1c2	85	Cao, D., Wang, J., Zhou, R. e
308	Flupenthixol	2709-56-0	FC(F)(F)c2cc1	100	Cao, D., Wang, J., Zhou, R. e
309	Diethylcarbamazine	90-89-1	O=C(N1CCN(	90	Therapeutic d EU/EF
310	Sulfamethoxazole	723-46-6	S(=O)(=O)(Nc	100	Cao, D., Wang, J., Zhou, R. e
311	Salicylic_Acid	69-72-7	Oc1ccccc1C(	100	Cao, D., Wang, J., Zhou, R. e
312	Celecoxib	169590-42-5	O=S(=O)(c3c	97	Paulson, S.K., I EF
313	Hydralazine	86-54-4	n1ncc2c(ccc	100	Cao, D., Wang, J., Zhou, R. e
314	Sparfloxacin	110871-86-8	Fc1c(N2CC(N	90	Cao, D., Wang, J., Zhou, R. e
315	Guanoxan	2165-19-7	O1c2c(OCC1	50	Cao, D., Wang, J., Zhou, R. e
316	Captopril	62571-86-2	SCC(C(=O)N1	84	Cao, D., Wang, J., Zhou, R. e
317	Fleroxacin	79660-72-3	CN1CCN(CC1	100	Varma, M. V. S., Obach, R. S
318	Dofetilide	115256-11-6	S(=O)(=O)(Nc	100	Cao, D., Wang, J., Zhou, R. e
319	Bisoprolol	66722-44-9	O(CC(O)CNC	96	Cao, D., Wang, J., Zhou, R. e
320	Cloxacillin	61-72-3	O=C(O)[C@@	75	Varma, M. V. S., Obach, R. S
321	Telmisartan	144701-48-4	OC(=O)c1ccc	50	Cao, D., Wang, J., Zhou, R. e
322	Propofol	2078-54-8	Oc1c(cccc1C	100	Cao, D., Wang, J., Zhou, R. e
323	Amrinone	60719-84-8	O=C1NC=C(C	93	Cao, D., Wang, J., Zhou, R. e
324	Meloxicam	71125-38-7	s1c(cnc1NC(=	90	Cao, D., Wang, J., Zhou, R. e
325	Mefenamic_Acid	61-68-7	OC(=O)c1ccc	90	Cao, D., Wang, J., Zhou, R. e
326	Brompheniramine_Maleate	86-22-6	Brc1ccc(cc1)	89	Cao, D., Wang, BA
327	Darifenacin hydrobromide	133099-04-4	c1ccc(cc1)C(	79	Skerjanec, A., EU/EF
328	Dextrose	50-99-7	O1C(CO)C(O	99	Cao, D., Wang, J., Zhou, R. e
329	Indacaterol maleate	312753-06-3	O=C4/C=C\c1	>45	Kagan M, Dain EF
330	Cilostazol	73963-72-1	O=C4Nc3c(c(	74	Chapman, T.M EU/EF
331	Phenylalanine	63-91-2	OC(=O)C(N)C	100	Cao, D., Wang, J., Zhou, R. e
332	Gestodene	60282-87-3	OC1(C=CC2C	100	Cao, D., Wang, J., Zhou, R. e
333	Ruxolitinib	941678-49-5	c1c[nH]c2c1(	95	Shilling AD, Ne EU/EF
334	Sulfapyridine	144-83-2	O=S(=O)(Nc1	70	Cao, D., Wang, J., Zhou, R. e
335	Bicalutamide	90357-06-5	S(=O)(=O)(C(	90	Cao, D., Wang, J., Zhou, R. e
336	Etodolac	41340-25-4	O1CCC2C(Nc	70	Cao, D., Wang, J., Zhou, R. e
337	Rofecoxib	162011-90-7	O=C2OCC(=C	93	Cao, D., Wang, BA
338	Nicotine	54-11-5	n1cc(ccc1)C1	100	Cao, D., Wang, J., Zhou, R. e
339	Tenoxicam	59804-37-4	s1c2C=C(N(S	100	Cao, D., Wang, J., Zhou, R. e
340	Gliclazide	21187-98-4	S(=O)(=O)(N(	97	Cao, D., Wang, J., Zhou, R. e
341	Pefloxacin	70458-92-3	Fc1cc2c(N(C3	100	Cao, D., Wang, J., Zhou, R. e
342	Tramadol	27203-92-5	O(C)c1cc(ccc	95	Cao, D., Wang, J., Zhou, R. e
343	Temocapril	111902-57-9	O=C(OCC)[C(	60	Püchler K, Sier EU/EF
344	Lorcaserin_Hydrochloride	616202-92-7	Cl.Clc1cc2c(c	92	Bays, H. E., Exp EU, REV
345	Voriconazole	137234-62-9	Fc1cncnc1[C	96	Cao, D., Wang, BA

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346	Fluorescein	2321-07-5	O1C2(c3c(cc	99	Cao, D., Wang, J., Zhou, R. e
347	Topiramate	97240-79-4	S(OCC12OC(	86	Cao, D., Wang, J., Zhou, R. e
348	Tinidazole	19387-91-8	S(=O)(=O)(C(	100	Cao, D., Wang, J., Zhou, R. e
349	Nevirapine	129618-40-2	O=C2Nc1c(c	100	Varma, M. V. S., Obach, R. S
350	Trovafloxacin	147059-72-1	Fc1cc(F)ccc1	88	Cao, D., Wang, J., Zhou, R. e
351	Glimepiride	93479-97-1	S(=O)(=O)(N(	100	Cao, D., Wang, J., Zhou, R. e
352	Enzalutamide	915087-33-1	FC(F)(F)c3cc(	85	http://www.a EU/EF
353	Quinine	130-95-0	O(c4cc1c(nc	85	Cao, D., Wang, J., Zhou, R. e
354	Pseudoephedrine	90-82-4	OC(C(NC)C)c	100	Cao, D., Wang, J., Zhou, R. e
355	Camazepam	36104-80-0	Clc1cc2c(N(C	100	Cao, D., Wang, J., Zhou, R. e
356	Papaverine	58-74-2	O(C)c1cc(ccc	90	Cao, D., Wang, J., Zhou, R. e
357	Aminopyrine	58-15-1	N(C)(C)C=1C	100	Cao, D., Wang, J., Zhou, R. e
358	Ketanserin	74050-98-9	Fc1ccc(cc1)C	100	Cao, D., Wang, J., Zhou, R. e
359	Phencyclidine	77-10-1	c1ccccc1C3(I	95	Varma, M. V. S., Obach, R. S
360	Ethionamide	536-33-4	S=C(N)c1cc(r	100	Cao, D., Wang, J., Zhou, R. e
361	Posaconazole	171228-49-2	CCC(C(C)O)n	96	Cao, D., Wang BA
362	Amphetamine	300-62-9	NC(Cc1ccccc	90	Cao, D., Wang, J., Zhou, R. e
363	Viloxazine	46817-91-8	O1CC(NCC1)	99	Cao, D., Wang, J., Zhou, R. e
364	Indobufen	63610-08-2	O=C1N(Cc2c	100	Cao, D., Wang, J., Zhou, R. e
365	Methylphenobarbital	115-38-8	O=C1N(C(=O	50	Cao, D., Wang, J., Zhou, R. e
366	Memantine	19982-08-2	NC12CC3(CC	100	Cao, D., Wang, J., Zhou, R. e
367	Betaxolol	63659-18-7	O(CC(O)CNC	90	Cao, D., Wang, J., Zhou, R. e
368	Praziquantel	55268-74-1	O=C1N2C(c3	96	Cao, D., Wang, J., Zhou, R. e
369	Loxoprofen	68767-14-6	O=C2C(Cc1c	58	Choo KS, Kim I EU
370	Flutamide	13311-84-7	FC(F)(F)c1cc(	100	Cao, D., Wang, J., Zhou, R. e
371	Methimazole	60-56-0	S=C1NC=CN1	95	Cao, D., Wang, J., Zhou, R. e
372	Valproic_Acid	99-66-1	OC(=O)C(CC(	98	Cao, D., Wang, J., Zhou, R. e
373	Tenidap	120210-48-2	Clc1cc2c(N(C	89	Cao, D., Wang, J., Zhou, R. e
374	Etoricoxib	202409-33-4	Clc1cc(c([n+]	100	Cao, D., Wang, J., Zhou, R. e
375	Glycine	56-40-6	OC(=O)CN	100	Cao, D., Wang, J., Zhou, R. e
376	Chlorzoxazone	95-25-0	Clc1cc2NC(C	90	Cao, D., Wang, J., Zhou, R. e
377	Omeprazole	73590-58-6	S(=O)(Cc1nc(	80	Cao, D., Wang, J., Zhou, R. e
378	Coumarin	91-64-5	O1c2c(C=CC1	100	Cao, D., Wang, J., Zhou, R. e
379	Codeine	76-57-3	O1C2C34C(C	95	Cao, D., Wang, J., Zhou, R. e
380	Biperiden	514-65-8	OC(CCN1CC(	100	Cao, D., Wang, J., Zhou, R. e
381	Isradipine	75695-93-1	o1nc2c(n1)c(	92	Cao, D., Wang, J., Zhou, R. e
382	Propylthiouracil	51-52-5	S=C1NC(=CC	90	Varma, M. V. S., Obach, R. S
383	Desmethyldiazepam	1088-11-5	Clc1cc2c(NC	99	Cao, D., Wang, J., Zhou, R. e
384	Ketotifen	34580-13-7	s1c2c(cc1)\C	90	Cao, D., Wang, J., Zhou, R. e
385	Oxazepam	604-75-1	Clc1cc2c(NC	97	Cao, D., Wang, J., Zhou, R. e
386	Mexiletine	31828-71-4	O(CC(N)C)c1	98	Cao, D., Wang, J., Zhou, R. e
387	Carnitine	541-15-1	C[N+](C)(C)C	10	Cao, D., Wang, J., Zhou, R. e
388	Ethambutol	74-55-5	OCC(NCCNC(	80	Cao, D., Wang, J., Zhou, R. e
389	Sirolimus	53123-88-9	O[C@@H]1C	>90	http://www.a EU-EF
390	Paroxetine	61869-08-7	Fc1ccc(cc1)C	100	Cao, D., Wang, J., Zhou, R. e
391	Pyridostigmine	155-97-5	O=C(Oc1ccc[	10	Varma, M. V. S., Obach, R. S
392	Imatinib	152459-95-5	O=C(Nc1cc(N	98	Cao, D., Wang, J., Zhou, R. e
393	Abacavir	168146-84-7	n3c1c(ncn1[I	83	Cao, D., Wang BA
394	Minocycline	10118-90-8	CN(C)[C@@H	100	Cao, D., Wang, J., Zhou, R. e
395	Famciclovir	104227-87-4	O(C(=O)C)CC	77	Cao, D., Wang, J., Zhou, R. e
396	Nitrofurantoin	67-20-9	o1c(ccc1[N+	95	Cao, D., Wang, J., Zhou, R. e
397	Mefloquine	53230-10-7	FC(F)(F)c1c2	78	Cao, D., Wang, J., Zhou, R. e
398	Pergolide_Mesilate	66104-23-2	S(C)C[C@@H	60	Therapeutic dı EF
399	Reboxetine	98769-81-4	O(c1ccccc1C	100	Varma, M. V. S., Obach, R. S
400	Pramipexole	104632-26-0	s1c2CC(NCC(	95	Cao, D., Wang, J., Zhou, R. e
401	Guanfacine	29110-47-2	Clc1cccc(Cl)c	100	Cao, D., Wang, J., Zhou, R. e
402	Nalbuphine	20594-83-6	O1C2C34CCI	100	Cao, D., Wang, J., Zhou, R. e
403	Itraconazole	84625-61-6	Clc1cc(Cl)ccc	80	Cao, D., Wang, J., Zhou, R. e
404	Nimodipine	66085-59-4	O=C(OC(C)C)	100	Cao, D., Wang, J., Zhou, R. e

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405	Galantamine	357-70-0	O1c2c3C4(C:	100	Cao, D., Wang, J., Zhou, R. e
406	Atomoxetine	83015-26-3	O(c1ccccc1C	100	Varma, M. V. S., Obach, R. S
407	Methysergide	361-37-5	OCC(NC(=O)(	100	Cao, D., Wang, J., Zhou, R. e
408	Metronidazole	443-48-1	OCCn1c(ncc:	95	Cao, D., Wang, J., Zhou, R. e
409	Olanzapine	132539-06-1	CN1CCN(CC1	100	Cao, D., Wang, J., Zhou, R. e
410	Tiagabine	115103-54-3	s1ccc(C)c1\C	95	Cao, D., Wang, J., Zhou, R. e
411	Venlafaxine	93413-69-5	O(C)c1ccc(cc	95	Cao, D., Wang, J., Zhou, R. e
412	Isoniazid	54-85-3	O=C(NN)c1c(	80	Cao, D., Wang, J., Zhou, R. e
413	Quetiapine	111974-69-7	S1c2c(cccc2)	73	Cao, D., Wang, J., Zhou, R. e
414	Propoxyphene	469-62-5	O(C(Cc1cccc(	95	Cao, D., Wang, J., Zhou, R. e
415	Tianeptine	66981-73-5	Clc1cc2S(=O)	99	Cao, D., Wang, J., Zhou, R. e
416	Mirtazapine	61337-67-5	n1cccc3c1N4	80	Varma, M. V. S., Obach, R. S
417	Ethosuximide	77-67-8	O=C1NC(=O)	93	Cao, D., Wang, BA
418	Ropinirole	91374-21-9	O=C1Nc2c(C	98	Cao, D., Wang, J., Zhou, R. e
419	Rivastigmine	123441-03-2	O(C(=O)N(CC	98	Cao, D., Wang, J., Zhou, R. e
420	Methylphenidate	113-45-1	O(C(=O)C(C1	80	Cao, D., Wang, J., Zhou, R. e
421	Zonisamide	68291-97-4	S(=O)(=O)(N)	100	Cao, D., Wang, J., Zhou, R. e
422	Hydrocodone	125-29-1	O=C4[C@@H	80	Cao, D., Wang, BA
423	Riluzole	1744-22-5	s1c2cc(OC(F)	90	Cao, D., Wang, J., Zhou, R. e
424	Perphenazine	58-39-9	Clc1cc2N(c3(	100	Cao, D., Wang, J., Zhou, R. e
425	Clonazepam	1622-61-3	Clc1ccccc1C:	100	Cao, D., Wang, J., Zhou, R. e
426	Fluvoxamine	54739-18-3	FC(F)(F)c1cc(	90	Cao, D., Wang, J., Zhou, R. e
427	Ramelteon	196597-26-9	O=C(NCC[C@	84	Cao, D., Wang, J., Zhou, R. e
428	Nortriptyline	72-69-5	N(CC\C=C/1\	100	Cao, D., Wang, J., Zhou, R. e
429	Rosiglitazone	122320-73-4	O=C1NC(=O)	100	Cao, D., Wang, J., Zhou, R. e
430	Oxybutynin	5633-20-5	O(C(=O)C(O)	100	Cao, D., Wang, J., Zhou, R. e
431	Moclobemide	71320-77-9	Clc1ccc(cc1)(	88	Cao, D., Wang, J., Zhou, R. e
432	Clomipramine	303-49-1	Clc1cc2N(c3(	95	Cao, D., Wang, J., Zhou, R. e
433	Zaleplon	151319-34-5	O=C(N(CC)c1	100	Cao, D., Wang, J., Zhou, R. e
434	Nitrazepam	146-22-5	O=C1Nc2c(c(	95	Cao, D., Wang, J., Zhou, R. e
435	Gemfibrozil	25812-30-0	O(CCCC(C(O)	100	Cao, D., Wang, J., Zhou, R. e
436	Trimipramine	739-71-9	N(CC(CN1c2(	80	Cao, D., Wang, J., Zhou, R. e
437	Lorcainide	59729-31-6	Clc3ccc(N(C(	70	Varma, M. V. S., Obach, R. S
438	Doxapram	309-29-5	O=C4N(CC)C	100	Varma, M. V. S., Obach, R. S
439	Maprotiline	10262-69-8	N(CCCC12CC	98	Cao, D., Wang, J., Zhou, R. e
440	Phenobarbital	50-06-6	O=C1NC(=O)	100	Cao, D., Wang, J., Zhou, R. e
441	Doxepin	1668-19-5	O1Cc2c(cccc	100	Cao, D., Wang, J., Zhou, R. e
442	Flumazenil	78755-81-4	Fc1cc2c(-n3(	95	Cao, D., Wang, J., Zhou, R. e
443	Bufuralol	54340-62-4	OC(c2oc1c(c	100	Varma, M. V. S., Obach, R. S
444	Procyclidine	77-37-2	OC(CCN1CC(	100	Cao, D., Wang, J., Zhou, R. e
445	Selegiline	14611-52-0	N(C(Cc1cccc(	100	Cao, D., Wang, J., Zhou, R. e
446	Flurazepam	17617-23-1	Clc1cc2c(N(C	100	Cao, D., Wang, J., Zhou, R. e
447	Nalidixic_Acid	389-08-2	O=C1c2ccc(n	90	Cao, D., Wang, J., Zhou, R. e
448	AAFC flurocitabine	37717-21-8	FC1=CN2C3C	32	Cao, D., Wang, J., Zhou, R. e
449	Acarbose	56180-94-0	O1C(C)C(NC2	2	Cao, D., Wang, J., Zhou, R. e
450	Acenocoumarol	152-72-7	[O-][N+](=O)	90	Therapeutic drugs, 2ed (19
451	Acetanilide	103-84-4	O=C(Nc1cccc(	83	Brodie, B. B. a EU-EF
452	Acetohexamide	968-81-0	S(=O)(=O)(\N	80	Cao, D., Wang, J., Zhou, R. e
453	Acipimox	51037-30-0	OC(=O)c1ncc(	95	Cao, D., Wang, J., Zhou, R. e
454	Acitretin	55079-83-9	O(C)c1cc(C)c	72	Cao, D., Wang, J., Zhou, R. e
455	Adefovir	106941-25-7	P(O)(O)(=O)(	16	Cao, D., Wang, J., Zhou, R. e
456	Adinazolam	37115-32-5	Clc3cc2\C(=N	100	Varma, M. V. S., Obach, R. S
457	Alcuronium	23214-96-2	OC\C=C/1\C:	0	Cao, D., Wang, J., Zhou, R. e
458	Alfacalcidol	41294-56-8	OC1CC(O)C\(	100	Cao, D., Wang, J., Zhou, R. e
459	Alizapride	59338-93-1	O=C(c2cc1nr	100	Varma, M. V. S., Obach, R. S
460	Allopurinol	315-30-0	O=C1NC=Nc:	80	Cao, D., Wang, J., Zhou, R. e
461	Almitrine	27469-53-0	Fc1ccc(cc1)C	90	Cao, D., Wang, J., Zhou, R. e
462	Almotriptan	154323-57-6	S(=O)(=O)(N:	75	Cao, D., Wang, J., Zhou, R. e
463	Alogliptin	850649-62-6	O=C1N(/C(=(	100	Andukuri, R., D EU/EF/BA

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464	Amikacin	37517-28-5	O1C(CN)C(O	0	Cao, D., Wang, J., Zhou, R. e
465	Aminoglutethimide	125-84-8	O=C1NC(=O)	100	Cao, D., Wang, J., Zhou, R. e
466	Amiodarone	1951-25-3	Ic1cc(cc(I)c1	100	Varma, M. V. S., Obach, R. S
467	Amobarbital	57-43-2	OC1=NC(O)=	95	Cao, D., Wang, J., Zhou, R. e
468	Amosulalol	85320-68-9	S(=O)(=O)(N)	100	Cao, D., Wang, J., Zhou, R. e
469	Amoxapine	14028-44-5	Clc1cc2c(Oc	95	Cao, D., Wang, J., Zhou, R. e
470	Anagrelide	68475-42-3	Clc1c2CN3C(	70	Cao, D., Wang, J., Zhou, R. e
471	Anastrozole	120511-73-1	n1cn(nc1)Cc	100	Cao, D., Wang, J., Zhou, R. e
472	Arbekacin	51025-85-5	O1C(CO)C(O	0	Cao, D., Wang, J., Zhou, R. e
473	Atovaquone	95233-18-4	O=C1c4cccc(	6	Varma, M. V. S., Obach, R. S
474	Atracurium	64228-79-1	O(C)c1cc(ccc	0	Cao, D., Wang, J., Zhou, R. e
475	Azatadine	3964-81-6	n1c/2c(CCc3	90	Cao, D., Wang, J., Zhou, R. e
476	Azathioprine	446-86-6	[O-][N+](=O)	87	Therapeutic dr EF/EU
477	Azelastine	58581-89-8	Clc1ccc(cc1)(	90	http://www.ac EF
478	Azimilide	149888-94-8	Clc1ccc(cc1)·	100	Cao, D., Wang, J., Zhou, R. e
479	Azlocillin	37091-66-0	S1C2N(C(C(C	0	Cao, D., Wang, J., Zhou, R. e
480	Azosemide	27589-33-9	O=S(=O)(N)c	20	Suh, O.K., Kim, REV/BA
481	Bambuterol	81732-65-2	O=C(Oc1cc(c	20	Cao, D., Wang, J., Zhou, R. e
482	Benserazide	322-35-0	Oc1c(O)c(O)(	70	Cao, D., Wang, J., Zhou, R. e
483	Benzbromarone	3562-84-3	Brc1cc(cc(Br	73	Cao, D., Wang, J., Zhou, R. e
484	Benzydamine	642-72-8	O(CCCN(C)C)	87	Cao, D., Wang, J., Zhou, R. e
485	Bepridil	64706-54-3	O(CC(C)C)CC	100	Cao, D., Wang, J., Zhou, R. e
486	Betahistine	5638-76-6	n1ccccc1CCN	100	Cao, D., Wang, J., Zhou, R. e
487	Betazole	105-20-4	n1ccc(n1)CC	100	Cao, D., Wang, J., Zhou, R. e
488	Bezafibrate	41859-67-0	O(C(C(O)=O)	100	Cao, D., Wang, J., Zhou, R. e
489	Bifemelane	90293-01-9	O(CCCCNC)c	95	Cao, D., Wang, J., Zhou, R. e
490	Biotin	58-85-5	S1CC2NC(=O	100	Cao, D., Wang, J., Zhou, R. e
491	Bornaprine	20448-86-6	O(C(=O)C1(C	100	Cao, D., Wang, J., Zhou, R. e
492	Bromfenac	91714-94-2	O=C(c1ccc(B	100	Varma, M. V. S., Obach, R. S
493	Bromhexine	3572-43-8	Brc1cc(Br)cc	70	Cao, D., Wang, J., Zhou, R. e
494	Buflomedil	55837-25-7	O=C(c1c(OC)	100	Varma, M. V. S., Obach, R. S
495	Bumetanide	28395-03-1	S(=O)(=O)(N)	96	Cao, D., Wang, J., Zhou, R. e
496	Bupivacaine	2180-92-9	O=C(Nc1c(cc	90	Varma, M. V. S., Obach, R. S
497	Busulfan	55-98-1	O=S(=O)(OC(	100	Cao, D., Wang, J., Zhou, R. e
498	Butylscopolamine	149-64-4	O1C2C3[N+]	10	Cao, D., Wang, J., Zhou, R. e
499	Canagliflozin	842133-18-0	Cc1ccc(cc1C	84	http://www.ac EU/BA
500	Candoxatril	118785-03-8	O=C(N[C@H	38	Beaumont, K., REV
501	Capecitabine	154361-50-9	FC1=CN(C2O	96	Cao, D., Wang, J., Zhou, R. e
502	Capreomycin	11003-38-6a	C[C@@H]1N	50	Cao, D., Wang, J., Zhou, R. e
503	Carbimazole	22232-54-8	S=C1N(C=CN	95	Cao, D., Wang, J., Zhou, R. e
504	Carboplatin	41575-94-4	C1CC2(C1)C(	77	Varma, M. V. S., Obach, R. S
505	Carfecillin	27025-49-6	S1C2N(C(C(C	99	Cao, D., Wang, J., Zhou, R. e
506	Carmustine	154-93-8	ClCCN(N=O)(	100	Cao, D., Wang, J., Zhou, R. e
507	Carprofen	53716-49-7	O=C(O)C(c3c	100	Cao, D., Wang, J., Zhou, R. e
508	Carteolol	51781-06-7	O(CC(O)CNC	95	Cao, D., Wang, J., Zhou, R. e
509	Cefcanel	41952-52-7	O=C2N1/C(=	42	Varma, M. V. S., Obach, R. S
510	Cefetamet	65052-63-3	O=C2N1/C(=	52	Varma, M. V. S., Obach, R. S
511	Cefetamet_Pivoxil	65243-33-6	s1cc(nc1N)/(	47	Cao, D., Wang, J., Zhou, R. e
512	Cefodizime	69739-16-8	s1c(CC(O)=O	0	Cao, D., Wang, J., Zhou, R. e
513	Ceforanide	60925-61-3	O=C2N1/C(=	0	Yalkowsky, S.H., Johnson, J.
514	Cefpirome	84957-29-9	s1cc(nc1N)/(	0	Cao, D., Wang, J., Zhou, R. e
515	Cefpodoxime_Proxetil	87239-81-4	s1cc(nc1N)/(	50	Cao, D., Wang, J., Zhou, R. e
516	Ceftizoxime	68401-81-0	s1cc(nc1N)/(	72	Cao, D., Wang, J., Zhou, R. e
517	Cefuroxime_Axetil	64544-07-6	S1C2N(C(=O)	44	Cao, D., Wang, J., Zhou, R. e
518	Celiprolol	56980-93-9	O(CC(O)CNC	50	Cao, D., Wang, J., Zhou, R. e
519	Chloral_Hydrate	302-17-0	ClC(Cl)(Cl)C(	100	Cao, D., Wang, J., Zhou, R. e
520	Chlorambucil	305-03-3	ClCCN(CCCl)(	100	Cao, D., Wang, J., Zhou, R. e
521	Chlordiazepoxide	58-25-3	Clc1cc2c(N=(	100	Cao, D., Wang, J., Zhou, R. e
522	Chlorguanide	500-92-5	Clc1ccc(NC(N	85	Cao, D., Wang, J., Zhou, R. e

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523	Chlorphenesin	104-29-0	Clc1ccc(OCC	100	Cao, D., Wang, J., Zhou, R. e
524	Chlorpropamide	94-20-2	Clc1ccc(S(=O	95	Cao, D., Wang, J., Zhou, R. e
525	Cibenzoline	53267-01-9	N\1=C(\NCC,	100	Varma, M. V. S., Obach, R. S
526	Cicaprost	94079-80-8	OC1CC2C(C\	100	Cao, D., Wang, J., Zhou, R. e
527	Cidofovir	113852-37-2	O=C1/N=C(\(	3	Cao, D., Wang, J., Zhou, R. e
528	Cilazapril	92077-78-6	O=C1N2N(C(	59	Cao, D., Wang, J., Zhou, R. e
529	Cilazaprilat	90139-06-3	O=C1N2N(C(	20	Cao, D., Wang, J., Zhou, R. e
530	Cilomilast	153259-65-5	O(c1cc(ccc1(	100	Cao, D., Wang, J., Zhou, R. e
531	Cinchonine	118-10-5	OC(C1N2CC(	100	Cao, D., Wang, J., Zhou, R. e
532	Cinoxacin	28657-80-9	O1c2c(OC1)(	95	Cao, D., Wang, J., Zhou, R. e
533	Ciprofibrate	52214-84-3	ClC1(Cl)CC1(	99	Cao, D., Wang, J., Zhou, R. e
534	Clavulanic_Acid	58001-44-8	O\1C2N(C(C(	73	Bolton, G.C, Al EU/EF
535	Clinafloxacin	105956-97-6	Fc2c(c(Cl)c1I	100	Varma, M. V. S., Obach, R. S
536	Clobazam	22316-47-8	Clc1cc2N(C(=	100	Cao, D., Wang, J., Zhou, R. e
537	Clofibrate	637-07-0	Clc1ccc(OC((	96	Cao, D., Wang, J., Zhou, R. e
538	Clomethiazole	533-45-9	ClCCc1scnc1	95	Cao, D., Wang, J., Zhou, R. e
539	Clopidogrel	113665-84-2	COC(=O)[C@	50	Cao, D., Wang, J., Zhou, R. e
540	Colestipol	50925-79-6	[NH3+]CC[NI	0	Cao, D., Wang, J., Zhou, R. e
541	Conivaptan	210101-16-9	O=C(c2ccccc	100	Varma, M. V. S., Obach, R. S
542	Cotinine	486-56-6	O=C1N(C)C((	97	Cao, D., Wang, J., Zhou, R. e
543	Cyclopenthiazide	742-20-1	Clc1cc2NC(N	100	Cao, D., Wang, J., Zhou, R. e
544	Cyclophosphamide	50-18-0	O=P1(OCCCN	82.5	Varma, M. V. S., Obach, R. S
545	Cyproheptadine	129-03-3	N1(CCC(CC1)	80	Cao, D., Wang, J., Zhou, R. e
546	Cyproterone_Acetate	427-51-0	ClC=1C2=CC(	98	Cao, D., Wang, J., Zhou, R. e
547	Cysteamine	60-23-1	SCCN	0	Cao, D., Wang, J., Zhou, R. e
548	Dalfampridine	504-24-5	n1ccc(N)cc1	100	Pikoulas, T.E., REV
549	Dantrolene	7261-97-4	o1c(ccc1\C=I	80	Cao, D., Wang, J., Zhou, R. e
550	Dapiprazole	72822-12-9	n1nc(n2c1CC	0	Cao, D., Wang, J., Zhou, R. e
551	Delapril	83435-66-9	O=C(OCC)[C(	45	Beaumont, K., REV
552	Delmopinol	79874-76-3	O1CC(N(CC1	95	Cao, D., Wang, J., Zhou, R. e
553	Desogestrel	54024-22-5	OC1(CCC2C3	72	Cao, D., Wang, J., Zhou, R. e
554	Dextromoramide	357-56-2	O1CCN(CC1)	100	Cao, D., Wang, J., Zhou, R. e
555	Diazoxide	364-98-7	Clc1cc2S(=O	90	Cao, D., Wang, J., Zhou, R. e
556	Dicyclomine	77-19-0	O(C(=O)C1(C	100	Cao, D., Wang, J., Zhou, R. e
557	Dienogest	65928-58-7	OC1(CCC2C3	94	Cao, D., Wang, J., Zhou, R. e
558	Diethylpropion	90-84-6	O=C(C(N(CC)	95	Cao, D., Wang, J., Zhou, R. e
559	Diethylstilbestrol	56-53-1	Oc1ccc(cc1)/	90	Cao, D., Wang, J., Zhou, R. e
560	Digitoxin	71-63-6	O1C(C)C(OC2	90	Cao, D., Wang, J., Zhou, R. e
561	Dihydrocodeine	125-28-0	O1C2C34C(C	89	Cao, D., Wang, J., Zhou, R. e
562	Dihydroergotamine	511-12-6	O1C(NC(=O)(	35	Cao, D., Wang, J., Zhou, R. e
563	Diloxanide	3736-81-0	ClC(Cl)C(=O)I	90	Cao, D., Wang, J., Zhou, R. e
564	Diphemanil	15394-62-4	[N+]1(CCC(C(	7	Cao, D., Wang, J., Zhou, R. e
565	Diprophylline	479-18-5	O=C2N(c1nc	95	Varma, M. V. S., Obach, R. S
566	Distigmine	15876-67-2	O(C(=O)N(CC	8	Cao, D., Wang, J., Zhou, R. e
567	Disulfiram	97-77-8	S(SC(=S)N(CC	97	Cao, D., Wang, J., Zhou, R. e
568	Dothiepin	113-53-1	S1Cc2c(cccc2	95	Cao, D., Wang, J., Zhou, R. e
569	Doxazosin	74191-85-8	O1c2c(OCC1	100	Cao, D., Wang, J., Zhou, R. e
570	Doxifluridine	3094-09-5	FC=1C(=O)N(	90	Varma, M. V. S., Obach, R. S
571	Drotaverine	985-12-6	O(c1ccc(cc1(	100	Varma, M. V. S., Obach, R. S
572	Eflornithine	67037-37-0	FC(F)C(N)(CC	55	Cao, D., Wang, J., Zhou, R. e
573	Eltrombopag_Olamine	496775-61-2	Cc1ccc(cc1C)	52	Deng, Y., Mad REV/EU
574	Encainide	66778-36-7	O=C(c1ccc(O	95	Varma, M. V. S., Obach, R. S
575	Enoximone	77671-31-9	S(C)c1ccc(cc	80	Cao, D., Wang, J., Zhou, R. e
576	Entecavir	142217-69-4	C=C3[C@H]((	100	Cao, D., Wang, J., Zhou, R. e
577	Epristeride	119169-78-7	CC(C)(C)NC(=	93	Varma, M. V. S., Obach, R. S
578	Eprosartan	133040-01-4	O=C(O)\C(=C	15	Varma, M. V. S., Obach, R. S
579	Ergoloid_Mesylate	8067-24-1	O=C6N7C(C((	25	Cao, D., Wang, J., Zhou, R. e
580	Ergotamine	113-15-5	O1C(NC(=O)(	100	Cao, D., Wang, J., Zhou, R. e
581	Erlotinib	183321-74-6	COCCOc1cc2	60	Cao, D., Wang, J., Zhou, R. e

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582	Estramustine	2998-57-4	ClCCN(CCCl)(	90	Varma, M. V. S., Obach, R. S
583	Ethacrynic_Acid	58-54-8	Clc1c(Cl)c(O(	90	Cao, D., Wang, J., Zhou, R. e
584	Ethanol	64-17-5	OCC	100	Cao, D., Wang, J., Zhou, R. e
585	Ethynodiol_Diacetate	297-76-7	O(C(=O)C)C1	100	Cao, D., Wang, J., Zhou, R. e
586	Etidronate	2809-21-4	P(O)(O)(=O)(	5	Cao, D., Wang, J., Zhou, R. e
587	Etilefrine	709-55-7	OC(c1cc(O)c(	100	Varma, M. V. S., Obach, R. S
588	Etravirine	269055-15-4	N#Cc3cc(c(O	16	Hussar, D.A. a REV/EF
589	Ezogabine	150812-12-7	O=C(OCC)Nc	84	Borlak, J., Gas EU
590	Febuxostat	144060-53-7	N#Cc1c(OCC	89	Grabowski, B./ EU/EF
591	Felbamate	25451-15-4	O(CC(COC(=(	90	Cao, D., Wang, J., Zhou, R. e
592	Fenclofenac	34645-84-6	Clc1cc(Cl)ccc	100	Cao, D., Wang, J., Zhou, R. e
593	Fenfluramine	458-24-2	FC(F)(F)c1cc(	95	Cao, D., Wang, J., Zhou, R. e
594	Fenofibrate	49562-28-9	O=C(c1ccc(C	90	Cao, D., Wang, J., Zhou, R. e
595	Fenspiride	5053-08-7	O=C3OC1(CC	100	Varma, M. V. S., Obach, R. S
596	Feprazone	30748-29-9	O=C1N(N(C(=	90	Cao, D., Wang, J., Zhou, R. e
597	Fidaxomicin	873857-62-6	Clc1c(c(c(O)(	8	http://www.a EF
598	Finasteride	98319-26-7	O=C1NC2CC(	100	Cao, D., Wang, J., Zhou, R. e
599	Flucloxacillin	5250-39-5	O=C(O)[C@(	80	Cao, D., Wang, J., Zhou, R. e
600	Flucytosine	2022-85-7	FC1=CNC(=O	100	Cao, D., Wang, J., Zhou, R. e
601	Fludrocortisone_Acetate	514-36-3	FC12C(C3CC(	95	Cao, D., Wang, J., Zhou, R. e
602	Flunarizine	52468-60-7	Fc1ccc(cc1)C	80	Cao, D., Wang, J., Zhou, R. e
603	Flunisolide	3385-03-3	FC1C2=CC(=(	80	Cao, D., Wang, J., Zhou, R. e
604	Fluoxymesterone	76-43-7	O=C4\C=C3/	44	Cao, D., Wang, J., Zhou, R. e
605	Flupirtine	56995-20-1	Fc1ccc(cc1)C	100	Varma, M. V. S., Obach, R. S
606	Fomepizole	7554-65-6	n1cc(cn1)C	100	Marraffa J, Forrest A, Grant
607	Fosfomycin	23155-02-4	P(O)(O)(=O)(	36	Cao, D., Wang, J., Zhou, R. e
608	Fosinopril	98048-97-6	P(OC(OC(=O)	35	Cao, D., Wang, J., Zhou, R. e
609	Fosmidomycin	66508-53-0	P(O)(O)(=O)(	30	Cao, D., Wang, J., Zhou, R. e
610	Frovatriptan	158747-02-5	O=C(N)c3ccc	40	Varma, M. V. S., Obach, R. S
611	Fructose	57-48-7	O1CC(O)C(O	100	Cao, D., Wang, J., Zhou, R. e
612	Fusidic_Acid	6990-06-3	O(C(=O)C)C/	100	Cao, D., Wang, J., Zhou, R. e
613	Gallopamil	16662-47-8	O(C)c1c(OC)(	97	Cao, D., Wang, J., Zhou, R. e
614	Gatifloxacin	112811-59-3	Fc1cc2c(N(C3	96	Cao, D., Wang, J., Zhou, R. e
615	Genaconazole	121650-83-7	S(=O)(=O)(C(	100	Cao, D., Wang, J., Zhou, R. e
616	Gentamicin_C1	1403-66-3	O1C(OC2C(O	0	Cao, D., Wang, J., Zhou, R. e
617	Gentamicin_C1A	548-62-9	O1C(OC2C(O	0	Cao, D., Wang, J., Zhou, R. e
618	Ginkgolide_A	15291-75-5	CC1C(=O)OC	90	Varma, M. V. S., Obach, R. S
619	Glibornuride	26944-48-9	S(=O)(=O)(N(	98	Cao, D., Wang, J., Zhou, R. e
620	Gliquidone	33342-05-1	S(=O)(=O)(N(	95	Cao, D., Wang, J., Zhou, R. e
621	Glycopyrrolate	596-51-0	O(C(=O)C(O)	18	Cao, D., Wang, J., Zhou, R. e
622	Glymidine	339-44-6	S(=O)(=O)(N(	95	Cao, D., Wang, J., Zhou, R. e
623	Granisetron	109889-09-0	O=C(NC1CC2	100	Cao, D., Wang, J., Zhou, R. e
624	Guanadrel	40580-59-4	O1C(COC12(	80	Cao, D., Wang, J., Zhou, R. e
625	Hexobarbital	56-29-1	OC1=NC(=O)	95	Cao, D., Wang, J., Zhou, R. e
626	Hydroflumethiazide	135-09-1	S(=O)(=O)(N)	67	Cao, D., Wang, J., Zhou, R. e
627	Hydromorphone hydrochloride	466-99-9	O=C4[C@@H	87	http://www.a EU-EF
628	Hydroxychloroquine	118-42-3	Clc1cc2nccc(	90	Cao, D., Wang, J., Zhou, R. e
629	Hydroxyprogesterone_Caproate	630-56-8	O(C(=O)CCC(	90	Cao, D., Wang, J., Zhou, R. e
630	Hydroxyurea	127-07-1	O=C(N)NO	100	Varma, M. V. S., Obach, R. S
631	Ibutilide	122647-31-8	S(=O)(=O)(N(	82	Cao, D., Wang, J., Zhou, R. e
632	Idazoxan	79944-56-2	O1c3c(OCC1	95	Varma, M. V. S., Obach, R. S
633	Ifosfamide	3778-73-2	O=P1(OCCCN	100	Varma, M. V. S., Obach, R. S
634	Imidapril	89396-94-1	O=C(O)[C@H	70	Cao, D., Wang, J., Zhou, R. e
635	Imipenem	74431-23-5	S(CC\N=C\N)	5	Cao, D., Wang, J., Zhou, R. e
636	Indecainide	74517-78-5	O=C(N)C3(c1	100	Cao, D., Wang, J., Zhou, R. e
637	Indoprofen	31842-01-0	O=C1N(Cc2c	100	Cao, D., Wang, J., Zhou, R. e
638	Iothalamatesodium	1225-20-3	Ic1c(C(=O)N(	2	Cao, D., Wang, J., Zhou, R. e
639	Isosorbide_Dinitrate	87-33-2	O1C2C(OCC2	90	Cao, D., Wang, J., Zhou, R. e
640	Isosorbide2Mononitrate	16051-77-7	O1C2C(OCC2	100	Cao, D., Wang, J., Zhou, R. e

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641	Isotretinoin	4759-48-2	OC(=O)\C=C(	90	Cao, D., Wang, J., Zhou, R. e
642	Isoxepac	55453-87-7	O1Cc2c(cccc	98	Cao, D., Wang, J., Zhou, R. e
643	Kanamycin	59-01-8	O1C(CNC(=O	1	Cao, D., Wang, J., Zhou, R. e
644	Ketazolam	27223-35-4	Clc1cc2c(N(C	100	Cao, D., Wang, J., Zhou, R. e
645	K-Strophanthoside	33279-57-1	O1C(COC2O(	16	Cao, D., Wang, J., Zhou, R. e
646	Lacidipine	103890-78-4	O(C(=O)C=1(	98	Cao, D., Wang, J., Zhou, R. e
647	Lacosamide	175481-36-4	O=C(N[C@@	100	http://www.a(BA
648	Lenalidomide	191732-72-6	O=C1NC(=O)	90	http://www.a(EU
649	Letrozole	112809-51-5	n1cn(nc1)C((	100	Cao, D., Wang, J., Zhou, R. e
650	Levamisole	14769-73-4	S1CCN2CC(N	95	Cao, D., Wang, J., Zhou, R. e
651	Levetiracetam	102767-28-2	O=C1N(CCC1	100	Cao, D., Wang, J., Zhou, R. e
652	Levobunolol	47141-42-4	O(CC(O)CNC	100	Cao, D., Wang, J., Zhou, R. e
653	Levomepromazine	60-99-1	O(c2cc1N(c3	53	Varma, M. V. S., Obach, R. S
654	Levonorgestrel	797-63-7	OC1(CCC2C3	100	Cao, D., Wang, J., Zhou, R. e
655	Levoprotiline	76496-68-9	O[C@@H](C	100	Varma, M. V. S., Obach, R. S
656	Levosimendan	141505-33-1	O=C1NN=C((	90	Cao, D., Wang, J., Zhou, R. e
657	Liothyronine	6893-02-3	O=C(O)C(N)C	95	Cao, D., Wang, J., Zhou, R. e
658	Lisuride	18016-80-3	O=C(NC1C=C	100	Cao, D., Wang, J., Zhou, R. e
659	Lodoxamide_Trometamol	63610-09-3	Clc1c(cc(C#N	70	Therapeutic drugs, 2ed (19
660	Lomustine	13010-47-4	O=C(NC1CCC	100	Cao, D., Wang, J., Zhou, R. e
661	Lormetazepam	848-75-9	Clc1ccccc1C1	100	Cao, D., Wang, J., Zhou, R. e
662	Lornoxicam	70374-39-9	Clc1sc2c(S(=(	100	Cao, D., Wang, J., Zhou, R. e
663	Loxiglumide	107097-80-3	Clc1ccc(C(=C	100	Varma, M. V. S., Obach, R. S
664	Lymecycline	992-21-2	OC(=O)[C@@	100	Cao, D., Wang, J., Zhou, R. e
665	Lynestrenol	52-76-6	OC1(CCC2C3	100	Cao, D., Wang, J., Zhou, R. e
666	Mebeverine	2753-45-9	O(C)c1cc(ccc	90	Cao, D., Wang, J., Zhou, R. e
667	Meclofenamic_Acid	644-62-2	Clc1c(Nc2cc(	100	Cao, D., Wang, J., Zhou, R. e
668	Megestrol_Acetate	3562-63-8	O(C(=O)C)C1	100	Cao, D., Wang, J., Zhou, R. e
669	Meperidine	57-42-1	O(C(=O)C1(C	100	Cao, D., Wang, J., Zhou, R. e
670	Meptazinol	54340-58-8	Oc1cc(ccc1)(	100	Cao, D., Wang, J., Zhou, R. e
671	Mercaptopurine	50-44-2	S=C2/N=C\N	50	Cao, D., Wang, J., Zhou, R. e
672	Meropenem	119478-56-7	S(C=1C(C2N(	0	Cao, D., Wang, J., Zhou, R. e
673	Mesna	19767-45-4	S(O)(=O)(=O)	77	Cao, D., Wang, J., Zhou, R. e
674	Mestranol	72-33-3	O(C)c1cc2CC	90	Cao, D., Wang, J., Zhou, R. e
675	Methocarbamol	532-03-6	O(CC(O)COC	100	Cao, D., Wang, J., Zhou, R. e
676	Methsuximide	77-41-8	O=C1N(C)C(=	100	Cao, D., Wang, J., Zhou, R. e
677	Methylergonovine	113-42-8	OCC(NC(=O)(	100	Cao, D., Wang, J., Zhou, R. e
678	Metyrapone	54-36-4	O=C(C(C)(C)c	80	Cao, D., Wang, J., Zhou, R. e
679	Mezlocillin	51481-65-3	S1C2N(C(C(C	0	Cao, D., Wang, J., Zhou, R. e
680	Mianserin	24219-97-4	N12C(c3c(Cc	70	Cao, D., Wang, J., Zhou, R. e
681	Miconazole	22916-47-8	Clc1cc(Cl)ccc	99	Cao, D., Wang, J., Zhou, R. e
682	Mifepristone	84371-65-3	OC1(CCC2C3	90	Cao, D., Wang, J., Zhou, R. e
683	Mifobate	76541-72-5	Clc1ccc(cc1)(	82	Cao, D., Wang, J., Zhou, R. e
684	Miglitol	72432-03-2	OCCN1[C@@	100	Cao, D., Wang The 100% va
685	Miglustat	72599-27-0	OC[C@H]1N	100	Cao, D., Wang, J., Zhou, R. e
686	Milrinone	78415-72-2	O=C1NC(C)=(	100	Cao, D., Wang, J., Zhou, R. e
687	Misoprostol	59122-46-2	OC1CC(=O)C	88	Cao, D., Wang, J., Zhou, R. e
688	Mitotane	53-19-0	Clc1ccccc1C(	40	Cao, D., Wang, J., Zhou, R. e
689	Mivacurium	106791-40-6	O(C)c1c(OC)(	0	Cao, D., Wang, J., Zhou, R. e
690	Modafinil	68693-11-8	S(=O)(C(c1cc	80	Cao, D., Wang, J., Zhou, R. e
691	Moexipril	103775-10-6	O=C(OCC)[C(	23	Beaumont, K., REV
692	Molsidomine	25717-80-0	o1n[n+](N2C	100	Cao, D., Wang, J., Zhou, R. e
693	Montelukast	158966-92-8	O=C(O)CC1((	80	Varma, M. V. S., Obach, R. S
694	Moricizine	31883-05-3	S1c2c(N(c3c1	88	Cao, D., Wang, J., Zhou, R. e
695	Moxalactam	64952-97-2	S(CC=1COC2	3	Cao, D., Wang, J., Zhou, R. e
696	Moxifloxacin	354812-41-2	Fc1cc2c(c(O(	90	Cao, D., Wang, J., Zhou, R. e
697	Moxisylyte	54-32-0	O(C(=O)C)c1(	70	Cao, D., Wang, J., Zhou, R. e
698	Moxonidine	75438-57-2	Clc1nc(nc(O(	88	Cao, D., Wang, J., Zhou, R. e
699	Mycophenolate_Mofetil	128794-94-5	O=C3OCc1c3	96.3	Bullingham RE REV

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700	Nabumetone	42924-53-8	O(C)c1cc2c(c	80	Cao, D., Wang, J., Zhou, R. e
701	Nafarelin	76932-56-4	NC(=O)CNC(=	0	Cao, D., Wang, J., Zhou, R. e
702	Nafronyl	31329-57-4	O1CCCC1CC(	100	Cao, D., Wang, J., Zhou, R. e
703	Naratriptan	121679-13-8	S(=O)(=O)(N(	70	Cao, D., Wang, J., Zhou, R. e
704	Nateglinide	105816-04-4	OC(=O)C(NC	83	Cao, D., Wang, J., Zhou, R. e
705	Nedocromil	69049-73-6	O1c2c(cc3c(I	3	Cao, D., Wang, J., Zhou, R. e
706	Nefazodone	83366-66-9	Clc1cc(N2CC	100	Cao, D., Wang, J., Zhou, R. e
707	Nefopam	13669-70-0	O1CCN(Cc2c	98	Cao, D., Wang, J., Zhou, R. e
708	Neomycin	1404-04-2	O1C(COC2C(	3	Cao, D., Wang, J., Zhou, R. e
709	Netilmicin	56391-56-1	O1C(=CC(N)(	0	Cao, D., Wang, J., Zhou, R. e
710	Niacin	59-67-6	c1cc(cnc1)C(	94	Cao, D., Wang, J., Zhou, R. e
711	Nicorandil	65141-46-0	O([N+](=O)[(	100	Cao, D., Wang, J., Zhou, R. e
712	Nilutamide	63612-50-0	FC(F)(F)c1cc(	100	Cao, D., Wang, J., Zhou, R. e
713	Nilvadipine	75530-68-6	O(C(=O)C=1(	100	Cao, D., Wang, J., Zhou, R. e
714	Nisoldipine	63675-72-9	O(C(=O)C=1(	90	Cao, D., Wang, J., Zhou, R. e
715	Nitroxoline	4008-48-4	Oc1c2ncccc2	100	Cao, D., Wang, J., Zhou, R. e
716	Nizatidine	76963-41-2	s1cc(nc1CN(	95	Cao, D., Wang, J., Zhou, R. e
717	Nomifensine	24526-64-5	c1ccc2c(c1N	100	Varma, M. V. S., Obach, R. S
718	Norgestimate	35189-28-7	O(C(=O)C)C1	100	Cao, D., Wang, J., Zhou, R. e
719	Orlistat	96829-58-2	O=C(O[C@H	17	http://www.a EF
720	Oxamniquine	21738-42-1	OCc1cc2CCC	80	Cao, D., Wang, J., Zhou, R. e
721	Oxatomide	60607-34-3	O=C1Nc2c(N	100	Cao, D., Wang, J., Zhou, R. e
722	Oxcarbazepine	28721-07-5	O=C(N)N1c2	100	Cao, D., Wang, J., Zhou, R. e
723	Oxiracetam	62613-82-5	O=C(N)CN1C	75	Varma, M. V. S., Obach, R. S
724	Oxitropium	30286-75-0	O1C2C3[N+]	16	Wahl D, van Wayjen RG, va
725	Oxyfedrine	15687-41-9	O(C)c1cc(ccc	85	Cao, D., Wang, J., Zhou, R. e
726	Oxyphenbutazone	129-20-4	Oc1ccc(N2N(	100	Cao, D., Wang, J., Zhou, R. e
727	Oxytetracycline	79-57-2	OC12C(C(N((	58	Cao, D., Wang, J., Zhou, R. e
728	Pafenolol	75949-61-0	O=C(NC(C)C)	29	Cao, D., Wang, J., Zhou, R. e
729	Pancuronium	16974-53-1	O(C(=O)C)C1	0	Cao, D., Wang, J., Zhou, R. e
730	Pantoprazole	102625-70-7	S(=O)(Cc1nc(	100	Cao, D., Wang, J., Zhou, R. e
731	Paromomycin	1263-89-4	O([C@H]3[C	0	Cao, D., Wang, J., Zhou, R. e
732	Pelrinone	94386-65-9	O=C1NC(=N(	98	Cao, D., Wang, J., Zhou, R. e
733	Penbutolol	36507-48-9	O(CC(O)CNC	100	Cao, D., Wang, J., Zhou, R. e
734	Penciclovir	39809-25-1	O=C2/N=C(\I	10	Varma, M. V. S., Obach, R. S
735	Pentazocine	359-83-1	Oc1cc2c(CC3	95	Cao, D., Wang, J., Zhou, R. e
736	Pentobarbital	76-74-4	O=C1NC(=O)	100	Cao, D., Wang, J., Zhou, R. e
737	Pentoxifylline	6493-05-6	O=C1N(CCCC	95	Cao, D., Wang, J., Zhou, R. e
738	Perhexiline	6621-47-2	N3C(CC(C1C(	80	Cao, D., Wang, J., Zhou, R. e
739	Perindopril_Erbumine	107133-36-8	O(C(=O)C(NC	95	Cao, D., Wang, J., Zhou, R. e
740	Phenacemide	63-98-9	O=C(NC(=O)I	100	Cao, D., Wang, J., Zhou, R. e
741	Phenglutarimide	1156-05-4	O=C1NC(=O)	100	Cao, D., Wang, J., Zhou, R. e
742	Phenindione	83-12-5	O=C1c2c(ccc	100	Cao, D., Wang, J., Zhou, R. e
743	Phenprocoumon	435-97-2	O1c2c(cccc2	95	Cao, D., Wang, J., Zhou, R. e
744	Phensuximide	86-34-0	O=C2N(C(=O	100	Cao, D., Wang, J., Zhou, R. e
745	Phenylpropanolamine	14838-15-4	OC(C(N)C)c1	95	Cao, D., Wang, J., Zhou, R. e
746	Phthalylsulfathiazole	85-73-4	s1ccnc1NS(=	5	Cao, D., Wang, J., Zhou, R. e
747	Physostigmine	57-47-6	O=C(Oc1cc2(	5	Varma, M. V. S., Obach, R. S
748	Pirbuterol	38029-10-6	Oc1ccc(nc1C	60	Cao, D., Wang, J., Zhou, R. e
749	Piretanide	55837-27-9	S(=O)(=O)(N)	85	Cao, D., Wang, J., Zhou, R. e
750	Pirmenol	68252-19-7	n1ccccc1C(O	95	Varma, M. V. S., Obach, R. S
751	Piroximone	84490-12-0	O=C1NC(C(=	81	Cao, D., Wang, J., Zhou, R. e
752	Pizotyline	15574-96-6	s1c2c(cc1)/C	80	Cao, D., Wang, J., Zhou, R. e
753	Polythiazide	346-18-9	Clc1cc2NC(N	100	Cao, D., Wang, J., Zhou, R. e
754	Pomalidomide	19171-19-8	O=C3NC(=O)	83	http://www.a EU-EF
755	Pralidoxime	6735-59-7	O\N=C\c1[n-	30	Cao, D., Wang, J., Zhou, R. e
756	Pranlukast	103177-37-3	O=C(c2ccc(O	20	Yoneda K, Matsumoto I, Su
757	Primidone	125-33-7	O=C1NCNC(=	95	Cao, D., Wang, J., Zhou, R. e
758	Probenecid	57-66-9	S(=O)(=O)(N(	100	Cao, D., Wang, J., Zhou, R. e

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759	Probucol	23288-49-5	S(c1cc(c(O)c	7	Cao, D., Wang, J., Zhou, R. e
760	Procainamide	51-06-9	O=C(c1ccc(N	85	Cao, D., Wang, J., Zhou, R. e
761	Procarbazine	671-16-9	O=C(NC(C)C)	100	Cao, D., Wang, J., Zhou, R. e
762	Propiverine	54556-98-8	O(C(=O)C(OC	84	Cao, D., Wang, J., Zhou, R. e
763	Prothionamide	14222-60-7	S=C(N)c1cc(r	100	Cao, D., Wang, J., Zhou, R. e
764	Protriptyline	438-60-8	N(CCCC1c2c	95	Cao, D., Wang, J., Zhou, R. e
765	Proxyphylline	603-00-9	O=C1N(C)C(=	100	Cao, D., Wang, J., Zhou, R. e
766	Pyrazinamide	98-96-4	O=C(N)c1ncc	100	Cao, D., Wang, J., Zhou, R. e
767	Pyrimethamine	58-14-0	Clc2ccc(c1c(	100	Cao, D., Wang, J., Zhou, R. e
768	Quinagolide	87056-78-8	S(=O)(=O)(N	100	Cao, D., Wang, J., Zhou, R. e
769	Quinalbarbitone	76-73-3	OC=1NC(=C)	90	Cao, D., Wang, J., Zhou, R. e
770	Quinapril	85441-61-8	O(C(=O)C(NC	60	Cao, D., Wang, J., Zhou, R. e
771	Quinaprilat	82768-85-2	O=C(O)[C@@	61	Varma, M. V. S., Obach, R. S
772	Rabeprazole	117976-89-3	S(=O)(Cc1nc	90	Cao, D., Wang, J., Zhou, R. e
773	Ramipril	87333-19-5	O(C(=O)C(NC	60	Cao, D., Wang, J., Zhou, R. e
774	Recainam	74738-24-2	O=C(Nc1c(cc	71	Cao, D., Wang, J., Zhou, R. e
775	Remoxipride	117591-79-4	Brc1ccc(OC)	100	Cao, D., Wang, J., Zhou, R. e
776	Reproterol	54063-54-6	Oc1cc(cc(O)	60	Cao, D., Wang, J., Zhou, R. e
777	Rimiterol	32953-89-2	Oc1cc(ccc1C	48	Cao, D., Wang, J., Zhou, R. e
778	Ritodrine	26652-09-5	Oc1ccc(cc1)(	95	Cao, D., Wang, J., Zhou, R. e
779	Rizatriptan	145202-66-0	[nH]1cc(c2cc	90	Cao, D., Wang, J., Zhou, R. e
780	Roquinimex	84088-42-6	CN(c1ccccc1	100	Varma, M. V. S., Obach, R. S
781	Rufinamide	106308-44-5	O=C(c1nnn(c	85	Perucca E, Clo REV
782	Saccharin	81-07-2	S1(=O)(=O)N	88	Cao, D., Wang, J., Zhou, R. e
783	Salbutamol	18559-94-9	OCc1cc(ccc1	83	Cao, D., Wang, J., Zhou, R. e
784	Salsalate	552-94-3	O(C(=O)c1cc	100	Cao, D., Wang, J., Zhou, R. e
785	Saxagliptin	361442-04-8	O=C(N1[C@H	75	http://www.a EU/EF
786	Sematilide	101526-62-9	O=S(=O)(Nc1	65	Varma, M. V. S., Obach, R. S
787	Sibutramine	106650-56-0	Clc1ccc(cc1)(	77	Cao, D., Wang, J., Zhou, R. e
788	Sitafloxacin	127254-12-0	F[C@H]5C[C	95	Varma, M. V. S., Obach, R. S
789	Sitagliptin	486460-32-6	Fc1cc(c(F)cc1	95	Varma, M. V. S., Obach, R. S
790	Solifenacin	242478-38-2	O=C(O[C@@	100	Varma, M. V. S., Obach, R. S
791	Spirapril	83647-97-6	O=C(OCC)[C(	60	Hayduk K and REV
792	Streptomycin	57-92-1	O1C(CO)C(O	1	Cao, D., Wang, J., Zhou, R. e
793	Streptozocin	18883-66-4	O1C(CO)C(O	21.5	Cao, D., Wang, J., Zhou, R. e
794	Succinylsulfathiazole	116-43-8	s1ccnc1NS(=	5	Cao, D., Wang, J., Zhou, R. e
795	Sudoxicam	34042-85-8	s1ccnc1NC(=	100	Cao, D., Wang, J., Zhou, R. e
796	Sufentanil	56030-54-7	O=C(N(c1ccc	90	Varma, M. V. S., Obach, R. S
797	Sulbactam	68373-14-8	S1(=O)(=O)C	5	Cao, D., Wang, J., Zhou, R. e
798	Sulfamethazine	57-68-1	S(=O)(=O)(N	95	Cao, D., Wang, J., Zhou, R. e
799	Sulfinpyrazone	57-96-5	S(=O)(CCC1C	100	Cao, D., Wang, J., Zhou, R. e
800	Sulfisomidine	515-64-0	S(=O)(=O)(N	90	Cao, D., Wang, J., Zhou, R. e
801	Sultopride	53583-79-2	S(=O)(=O)(CC	89	Kobari T, Nam EU
802	Suprofen	40828-46-4	O=C(c1ccc(c	92	Varma, M. V. S., Obach, R. S
803	Suramin	145-63-1	O=C(Nc1cc(c	0	Varma, M. V. S., Obach, R. S
804	Tamsulosin	106133-20-4	S(=O)(=O)(N)	100	Cao, D., Wang, J., Zhou, R. e
805	Tapentadol	175591-23-8	Oc1cc(ccc1)[	99	Terlinden, R., (EU
806	Teicoplanin_A2_1	91032-34-7	Clc1c2Oc3cc	0	Cao, D., Wang, J., Zhou, R. e
807	Temazepam	846-50-4	Clc1cc2c(N(C	95	Cao, D., Wang, J., Zhou, R. e
808	Temozolomide	85622-93-1	O=C(c1ncn2(	100	Cao, D., Wang, J., Zhou, R. e
809	Terodiline	15793-40-5	c1ccccc1C(c2	100	Varma, M. V. S., Obach, R. S
810	Tesaglitazar	251565-85-2	S(Oc1ccc(cc1	100	Cao, D., Wang, J., Zhou, R. e
811	Thiabendazole	148-79-8	s1cc(nc1)-c1	90	Cao, D., Wang, J., Zhou, R. e
812	Thioridazine	50-52-2	S(c2cc1N(c3(	60	Cao, D., Wang, J., Zhou, R. e
813	Tibolone	5630-53-5	OC1(CCC2C3	90	Cao, D., Wang, J., Zhou, R. e
814	Ticarcillin	34787-01-4	S1C2N(C(C(C	0	Cao, D., Wang, J., Zhou, R. e
815	Ticlopidine	55142-85-3	Clc1ccccc1Cl	80	Cao, D., Wang, J., Zhou, R. e
816	Tilidine	51931-66-9	O=C(CCC)C1(	100	Cao, D., Wang, J., Zhou, R. e
817	Tizanidine	51322-75-9	Clc1ccc3nsn(	100	Varma, M. V. S., Obach, R. S

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818	Tobramycin	32986-56-4	O1C(CO)C(O	0	Cao, D., Wang, J., Zhou, R. e
819	Tocainide	41708-72-9	O=C(Nc1c(cc	100	Cao, D., Wang, J., Zhou, R. e
820	Tolazoline	59-98-3	N1CCN=C1C	90	Cao, D., Wang, J., Zhou, R. e
821	Tolmesoxide	38452-29-8	S(=O)(C)c1cc	98	Cao, D., Wang, J., Zhou, R. e
822	Tolrestat	82964-04-3	S=C(N(CC(O)	66	Cao, D., Wang, J., Zhou, R. e
823	Tolterodine	124937-51-5	Oc1ccc(cc1C	77	Cao, D., Wang, J., Zhou, R. e
824	Toremifene	89778-26-7	ClCC\C(=C(\c	100	Cao, D., Wang, J., Zhou, R. e
825	Torsemide	56211-40-6	S(=O)(=O)(N(	96	Cao, D., Wang, J., Zhou, R. e
826	Trandolapril	87679-37-6	O(C(=O)C(NC	50	Cao, D., Wang, J., Zhou, R. e
827	Trapidil	15421-84-8	n12ncnc1N=	96	Cao, D., Wang, J., Zhou, R. e
828	Triamcinolone	124-94-7	FC12C(C3CC	100	Cao, D., Wang, J., Zhou, R. e
829	Triamcinolone_Acetonide	76-25-5	FC12C(C3CC	90	Cao, D., Wang, J., Zhou, R. e
830	Trifluoperazine	117-89-5	S1c2c(N(c3c	100	Cao, D., Wang, J., Zhou, R. e
831	Trihexyphenidyl	144-11-6	OC(CCN1CC(	100	Cao, D., Wang, J., Zhou, R. e
832	Trimeprazine	84-96-8	S1c2c(N(c3c	80	Cao, D., Wang, J., Zhou, R. e
833	Trofosfamide	22089-22-1	ClCCN1P(OC	100	Cao, D., Wang, J., Zhou, R. e
834	Tropisetron	89565-68-4	CN4[C@@H]	95	Cao, D., Wang, J., Zhou, R. e
835	Tubocurarine	57-95-4	O1c2cc3C([N	0	Cao, D., Wang, J., Zhou, R. e
836	Urapidil	34661-75-1	O(C)c1ccccc1	100	Varma, M. V. S., Obach, R. S
837	Vancomycin	1404-90-6	Clc1c2Oc3cc	0	Cao, D., Wang, J., Zhou, R. e
838	Varenicline tartrate	375815-87-5	n1c2cc3c(cc2	92	Obach RS, Ree EU
839	Vecuronium	50700-72-6	O(C(=O)C)C1	0	Cao, D., Wang, J., Zhou, R. e
840	Vigabatrin	60643-86-9	O=C(O)CCC(\	100	Cao, D., Wang, J., Zhou, R. e
841	Vilazodone	163521-12-8	Cl.N#Cc1ccc2	98	Frampton JE., REV/EF/EU
842	Vitamin_A	68-26-8	OC\C=C(\C=C	80	Cao, D., Wang, J., Zhou, R. e
843	Vitamin_E	59-02-9	Cc1c(c2c(c(c	65	Cao, D., Wang, J., Zhou, R. e
844	Ximoprofen	56187-89-4	OC(=O)C(C)c	98	Cao, D., Wang, J., Zhou, R. e
845	Xipamide	14293-44-8	O=S(=O)(c1c	80	Therapeutic drugs, 2ed (19
846	Zalcitabine	7481-89-2	O1C(CCC1N1	85	Cao, D., Wang, J., Zhou, R. e
847	Zanamivir	139110-80-8	O1C(C(O)C(C	2	Cao, D., Wang, J., Zhou, R. e
848	Zatebradine	85175-67-3	O(C)c1cc(ccc	79	Cao, D., Wang, J., Zhou, R. e
849	Zileuton	132880-11-6	s1c2c(cc1C(N	100	Cao, D., Wang, J., Zhou, R. e
850	Zopiclone	43200-80-2	Clc1ccc(nc1)	98	Cao, D., Wang, J., Zhou, R. e
851	Zotepine	26615-21-4	Clc1cc2c(Sc3	100	Cao, D., Wang, J., Zhou, R. e
852	Auranofin	34031-32-8	CC(=O)OC[C(	>23	Therapeutic dı EU
853	Ethylmorphine	76-58-4	O1C2C34C5(	48	Hedenmalm K, EU
854	Isocarboxazid	59-63-2	o1nc(cc1C)C	56	Koechlin,BA., S EU
855	Vismodegib	879085-55-9	CS(=O)(=O)c2	69.3	Graham RA, Lu EF
856	Apricitabine	160707-69-7	O=C1/N=C(/N	80	Cao, D., Wang BA
857	Clenbuterol	37148-27-9	Clc1cc(cc(Cl)	80	Cao, D., Wang BA
858	Etofylline	519-37-9	O=C2N(c1nc	80	Cao, D., Wang BA
859	Flunitrazepam	1622-62-4	[O-][N+](=O)	80	Cao, D., Wang BA
860	Leflunomide	75706-12-6	O=C(Nc1ccc(	80	Cao, D., Wang BA
861	Trimethobenzamide	138-56-7	O=C(c1cc(OC	80	Cao, D., Wang BA
862	Desvenlafaxine_Succinate	93413-62-8	OC2(C(c1ccc	80.5	Parker, VD., Ri BA
863	Sulfamerazine	127-79-7	O=S(=O)(Nc1	81	Cao, D., Wang BA
864	Chlorthalidone	77-36-1	Clc1ccc(cc1S	82	Varma, M. V. S BA
865	Mepindolol	23694-81-7	OC(CNC(C)C)	82	Cao, D., Wang BA
866	Mycophenolic_Acid	24280-93-1	O=C1OCc2c1	82.5	Cao, D., Wang BA
867	N_Acetylprocainamide	32795-44-1	O=C(Nc1ccc(	83	Cao, D., Wang BA
868	Pioglitazone	111025-46-8	O=C1NC(=O)	83	Cao, D., Wang BA
869	Valdecoxib	81695-72-7	O=S(=O)(N)c	83	Cao, D., Wang BA
870	Aprindine	37640-71-4	c1cccc3c1CC	85	Cao, D., Wang BA
871	Delavirdine	136817-59-9	O=S(=O)(Nc1	85	Cao, D., Wang BA
872	Norfenfluramine	1886-26-6	FC(F)(F)c1cc(	85	Cao, D., Wang BA
873	Aripiprazole	129722-12-9	Clc4cccc(N3(	87	Cao, D., Wang BA
874	Clindamycin	18323-44-9	ClC(C(NC(=O	87	Cao, D., Wang BA
875	Chloroxine	773-76-2	Clc1c(O)c2nc	89	Cao, D., Wang BA
876	Glyceryl1Nitrate	624-43-1	OCC(O)CO[N	89	Cao, D., Wang BA

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877	Carbazepine10_11Epoxide		NC(=O)N1C2	90	Cao, D., Wang, BA
878	Clomifene	911-45-5	Cl/C(c1ccccc	90	Cao, D., Wang, BA
879	Droxidopa	23651-95-8	O=C(O)C(N)C	90	Cao, D., Wang, BA
880	Ertapenem	153832-46-3	O=C(O)c1cc(	90	Cao, D., Wang, BA
881	Nitisinone	104206-65-7	O=C(c1ccc(c	90	Cao, D., Wang, BA
882	Fluocortolone	152-97-6	O=C\1\C=C/[	90	Cao, D., Wang, BA
883	Indapamide	26807-65-8	O=S(=O)(N)c	90	Cao, D., Wang, BA
884	Lofexidine	31036-80-3	Clc2c(OC(C/	90	Cao, D., Wang, BA
885	Toliprolol	2933-94-0	O(c1cc(ccc1)	90	Cao, D., Wang, BA
886	Clorazepate	23887-31-2	Clc3cc\1c(N(	91	Cao, D., Wang, BA
887	Phenylethylmalonamide	7206-76-0	CCC(C(N)=O)	91	Cao, D., Wang, BA
888	Emtricitabine	143491-57-0	FC=1\C(=N/C	93	Cao, D., Wang, BA
889	Estazolam	29975-16-4	Clc3cc2\C(=N	93	Cao, D., Wang, BA
890	Mazindol	22232-71-9	Clc1ccc(cc1)C	93	Cao, D., Wang, BA
891	Midodrine	133163-28-7	O=C(NCC(O)C	93	Cao, D., Wang, BA
892	Pipemidic_Acid	51940-44-4	O=C(O)\C2=C(	93	Cao, D., Wang, BA
893	Pirazolac	71002-09-0	Clc3ccc(c1cn	93.5	Cao, D., Wang, BA
894	Cefprozil	92665-29-7	O=C2N1/C(=	95	Therapeutic dr BA
895	Cinolazepam	75696-02-5	Fc3ccccc3C/	95	Cao, D., Wang, BA
896	Gitoxin	4562-36-1	O=C\1OC/C(	95	Cao, D., Wang, BA
897	Zuclopenthixol	53772-83-1	Clc2cc1C(\c3	95	Therapeutic dr BA
898	Oxandrolone	53-39-4	O=C3OC[C@	97	Cao, D., Wang, BA
899	Palonosetron	135729-61-2	O=C5N([C@H	97	Cao, D., Wang, BA
900	Treosulfan	299-75-2	O=S(=O)(OC(	97	Cao, D., Wang, BA
901	Antrafenine	55300-29-3	FC(F)(F)c5cc(	100	Cao, D., Wang, BA
902	Chlormezanone	80-77-3	O=S2(=O)CC(	100	Cao, D., Wang, BA
903	Cicloprolol	63659-12-1	O(c1ccc(OCC	100	Cao, D., Wang, BA
904	Amifostine	20537-88-6	O=P(O)(O)SC	100	Cao, D., Wang, BA
905	Benorylate	5003-48-5	O(C(=O)C)c1(	100	Cao, D., Wang, J., Zhou, R. e
906	Calcitriol	32222-06-3	O[C@@H]1C	100	Therapeutic drugs, 2ed (19
907	Chenodeoxycholic_Acid	474-25-9	C[C@H](CCC	100	Therapeutic drugs, 2ed (19
908	Oxtriphylline	146-71-4	[O-]/C2=C1\[	100	Cao, D., Wang, BA
909	Ursodeoxycholic_Acid	128-13-2	O=C(O)CCC(C	100	Therapeutic drugs, 2ed (19
910	Ezetimibe	163222-33-1	Fc1ccc(cc1)[C	>31	Patrick JE, Kos EU, EF, EUB
911	Carglumic _Acid	1188-38-1	O=C(O)CC[C(	>40	http://www.a EF
912	Deferasirox	201530-41-8	OC(=O)c1ccc	81	Waldmeier F, I BA, EU, EF
913	Ticagrelor	274693-27-5	Fc1ccc(cc1F)	>73	Teng R, Oliver EU, EF, EUB
914	Tetrabenazine	58-46-8	O(C)c1cc2C3	>75	http://www.a EU
915	Altretamine	645-05-6	n1c(nc(nc1N	>87	Ames MM, Po EU
916	Amdinocillin	32887-01-7	O=C(O)[C@@	Poor	Cao, D., Wang, J., Zhou, R. e
917	Amygdalin	29883-15-6	O1C(COC2OC	Poor	Cao, D., Wang, J., Zhou, R. e
918	Bephenium	7181-73-9	O(CC[N+](Cc	Poor	Cao, D., Wang, J., Zhou, R. e
919	Bethanechol	674-38-4	O(C(C[N+](C)	Poor	Cao, D., Wang, J., Zhou, R. e
920	Chlorhexidine	55-56-1	Clc1ccc(NC(N	Poor	Cao, D., Wang, J., Zhou, R. e
921	Diatrizoate	117-96-4	Ic1c(C(O)=O)	Poor	Cao, D., Wang, J., Zhou, R. e
922	Edetic_Acid/EDTA	60-00-4	OC(=O)CN(C	Poor	Bradberry S, Vale A., Clin To
923	Iohexol	66108-95-0	Ic1c(C(=O)NC	Poor	Cao, D., Wang, J., Zhou, R. e
924	Iotroxate	72704-51-9	O=C(Nc1c(c(	Poor	Therapeutic drugs, 2ed (19
925	Iotroxic_Acid	51022-74-3	Ic1c(C(O)=O)	Poor	Cao, D., Wang, J., Zhou, R. e
926	Ipratropium	60205-81-4	O(C(=O)C(CC	Poor	Cao, D., Wang, J., Zhou, R. e
927	Obidoxime	114-90-9	O(C[n+]1ccc(	Poor	Cao, D., Wang, J., Zhou, R. e
928	Pamidronic_Acid	40391-99-9	P(O)(O)(=O)C	Poor	Cao, D., Wang, J., Zhou, R. e
929	Pentolinium	52-62-0	[N+]1(CCCC1	Poor	Cao, D., Wang, J., Zhou, R. e
930	Poldine	596-50-9	O(CC1[N+](C	Poor	Cao, D., Wang, J., Zhou, R. e
931	Propantheline	298-50-0	O1c2c(cccc2	Poor	Cao, D., Wang, J., Zhou, R. e
932	Terlipressin	14636-12-5	O=C(N)CNC(=	Poor	Therapeutic drugs, 2ed (19

Caco-2 Papp permeability x10-6 cm/s (A-B)	*Caco-2 Reference*	*Perm comments*	*MDCK Papp permeability x10-6 cm/s (A-B)*	*MDCK Reference*	*Perm comments*
0.07	Sherer, EC., Verras, A., M		0.048	Irvine JD, Takahashi	MDCK (Strain
0.08	Pham The, H., González-/		0.1	Wang Q, Rager JD, \	MDR1-MDCK I
0.54	Skolnik S, Lin X, Wang J.,		0.1	Wang Q, Rager JD, \	MDR1-MDCK I
0.14	Pham The, H., González-/		0.15	Irvine JD, Takahashi	MDCK (Strain
4.34	Skolnik S, Lin X, Wang J.,		0.18	Wang Q, Rager JD, \	MDR1-MDCK I
2.30	Pham The, H., González-/		0.19	Varma MV, Sateesh	MDR1-MDCK I
1.1	Irvine JD, Takahashi L, Lo		0.22	Wang Q, Rager JD, \	MDR1-MDCK
0.43	Sherer, EC., Verras, A., M		0.24	Irvine JD, Takahashi	MDCK (Strain
1	Pham The, H., González-/		0.25	Varma MV, Sateesh	MDR1-MDCK I
0.315	Tavelin, S., Taipalensuu, .		0.255	Irvine JD, Takahashi	MDCK (Strain
4.20	Pham The, H., González-/		0.26	Liu W, Okochi H, Be	MDCK II
1.05	de Souza J, Benet LZ, Hua		0.27	de Souza J, Benet LZ	MDR1-MDCK
0.52	Pham The, H., González-/		0.3	Wager , TT., Chandr	MDR1-MDCK (
0.66	Skolnik S, Lin X, Wang J.,		0.34	Irvine JD, Takahashi	MDCK II/ MDC
12	Oo C, Snell P, Barrett J., e		0.35	Wen, G., Jia, R., Kar	MDR1-MDCK (
2.74	Jezyk N, Li C, Stewart BH.		0.36	Irvine JD, Takahashi	MDCK (Strain
1.38	Pham The, H., González-/		0.450	Varma MV, Gardner	MDR1-MDCK
4.37	Pham The, H., González-/		0.47	Nožinić,a, N., Milić,a	MDCK II
1.22	Pham The, H., González-/		0.5	Varma MV, Gardner	MDCK II
0.34	Pham The, H., González-/		0.55	Irvine JD, Takahashi	MDR1-MDCK
0.71	Skolnik S, Lin X, Wang J.,		0.6	Varma MV, Gardner	MDCK II
1.855	Skolnik S, Lin X, Wang J.,		0.6	Varma MV, Gardner	MDR1-MDCK
1.92	Pham The, H., González-/		0.6745	Varma MV, Sateesh	MDR1-MDCK
0.7	Crivori , P., Reinach, B. , F		0.69	Varma MV, Sateesh	MDR1-MDCK
0.405	Rege BD, Yu LX, Hussain /		0.7	Varma MV, Gardner	MDCKII
0.74	Thomas S, Brightman F, (		0.7	Varma MV, Gardner	MDCK II
1.13	Pham The, H., González-/		0.7	Varma MV, Gardner	MDCK II
3.62	Biganzoli E, Cavenaghi LA		0.7	Ranaldi, G., Islam, K	MDCK II
4.20	Fossati L, Dechaume R, H		0.7	Varma MV, Gardner	MDCK II
1.4	Skolnik S, Lin X, Wang J.,		0.7	Irvine JD, Takahashi	MDCK II/ Strai
0.31	Irvine JD, Takahashi L, Lo		0.73	Irvine JD, Takahashi	MDCK II/ MDC
0.22	Hua WJ, Fan Concentratic		0.82	Huang L, Wang Y, G	MDR1-MDCK (
1.66	Pham The, H., González-/		0.855	Varma MV, Gardner	MDR1-MDCK
0.466	Korjamo T, Honkakoski P		0.86	Lal R, Sukbuntherng	MDCK (Strain
0.466	Rege BD, Yu LX, Hussain /		0.86	Irvine JD, Takahashi	MDCK II/ MDC
7.64	Pham The, H., González-/		0.9	Varma MV, Gardner	MDCK II
0.24	Pham The, H., González-/		0.91	Irvine JD, Takahashi	MDCK (Strain
0.65	Pham The, H., González-/		0.95	Irvine JD, Takahashi	MDCK II/ MDC
0.41	Pham The, H., González-/		0.98	Varma MV, Sateesh	MDR1-MDCK
0.82	Skolnik S, Lin X, Wang J.,		1	Varma MV, Sateesh	MDR1-MDCK I
2.38	Skolnik S, Lin X, Wang J.,		1	Irvine JD, Takahashi	MDCK (Strain
2.19	Sherer, EC., Verras, A., M		1.1	Wager , TT., Chandr	MDR1-MDCK (
0.408	Yazdanian, M., Glynn, SL.		1.19	Irvine JD, Takahashi	MDR1-MDCK
0.24	Pham The, H., González-/		1.2	Varma MV, Gardner	MDCK II
6.92	Bachmakov concentratic		1.2	Varma MV, Gardner	MDCK II
2.51	Pham The, H., González-/		1.27	Irvine JD, Takahashi	MDR1-MDCK I
0.23	Skolnik S, Lin X, Wang J.,		1.325	Varma MV, Gardner	MDR1-MDCK I
4.83	Pham The, H., González-/		1.4	Varma MV, Gardner	MDCK II
6.8	Pham The, H., González-/		1.4	Irvine JD, Takahashi	MDCK (Strain
0.25	Sherer, EC., Verras, A., M		1.45	Varma MV, Sateesh	MDR1-MDCK I

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1.63	Pham The, H., González-/	1.45	Irvine JD, Takahashi MDCK II
3.69	Pham The, H., González-/	1.5	Varma MV, Gardner MDCK II
3.45	Pham The, H., González-/	1.7	Irvine JD, Takahashi MDCK (Strain
0.88	Pham The, H., González-/	1.8	Varma MV, Gardner MDCK II
2.23	Pham The, H., González-/	1.8	Varma MV, Gardner MDCK II
3.80	Pham The, H., González-/	1.85	Varma MV, Sateesh MDR1-MDCK
2.8	Ingels, F., Oth, M., Augus	1.9	Feng B, Mills JB, Dav MDCK (strain
0.20	Pham The, H., González-/	2.1	Varma MV, Gardner MDCK II
0.64	Skolnik S, Lin X, Wang J.,	2.14	Varma MV, Sateesh MDR1-MDCK
1.90	Pham The, H., González-/	2.2	Irvine JD, Takahashi MDCK (Strain
4.24	Teksin, ZS., Seo, PR., Polli	2.4	Varma MV, Gardner MDCK II
21.60	Pham The, H., González-/	2.525	Varma MV, Sateesh MDR1-MDCK
2.31	Zhu C, Jiang L, Chen TM,	2.7	Varma MV, Gardner MDCK II
27	Frick A., Helga Mo, H., W	2.7	Varma MV, Gardner MDCK II
2.37	Skolnik S, Lin X, Wang J.,	2.77	Varma MV, Gardner MDR1-MDCK I
10.10	Pham The, H., González-/	2.77	http://www.cypro MDR1-MDCK
11.24	Skolnik S, Lin X, Wang J.,	2.85	Varma MV, Sateesh MDR1-MDCK
33.97	Pham The, H., González-/	3.15	Refsgaard HH, Jense MDCK I
38.30	Pham The, H., González-/	3.5	http://www.cypro MDR1-MDCK I
125.70	Pham The, H., González-/	3.57	Wang Q, Rager JD, V MDR1-MDCK
1.05	Pham The, H., González-/	3.6	Huang L, Berry L, Ga MDCK (Strain
3.4	Sherer, EC., Verras, A., M	3.67	Varma MV, Sateesh MDR1-MDCK
2.73	Pham The, H., González-/	3.8	Varma MV, Gardner MDCK II
6.58	Pham The, H., González-/	3.9	Putnam WS, Pan L, " Strain not spe
9.6	http://www Saturation o	3.93	http://www.accesso Average of dif
12.95	Pham The, H., González-/	4.3	Varma MV, Gardner MDCK II
16.10	Pham The, H., González-/	4.6	Varma MV, Gardner MDCK II
11.15	Augustijns PF., J Pharm P	4.795	Varma MV, Gardner MDR1-MDCK
3.90	Pham The, H., González-/	4.99	Varma MV, Gardner MDR1-MDCK
11.75	Pham The, H., González-/	5	Varma MV, Gardner MDCK II
9.5	Gertz M, Harrison A, Hou	5.2	Gertz M, Harrison A MDR1-MDCK
3.60	Pham The, H., González-/	5.5	Varma MV, Gardner MDCK II
28.25	Faassen, F., Kelder, J., Le	5.73	Kim WY, Benet LZ., Pharm Res. 20(
6.53	Pham The, H., González-/	6.1	Varma MV, Gardner MDCK II
13.1	Gertz M, Harrison A, Hou	6.1	Varma MV, Gardner MDCK II
19.8	Pham The, H., González-/	6.1	Varma MV, Gardner MDCK II
7.1	Faassen, F., Kelder, J., Le	6.33	Kim WY, Benet LZ., I MDCK (strain
15.89	Skolnik S, Lin X, Wang J.,	6.8	Wager , TT., Chandr MDR1-MDCK
29.2	Gertz M, Harrison A, Hou	7.6	Varma MV, Gardner MDCK II
6.24	Lu Z, Chen W at ph 5.8	8.15	Luo S, Wang Z, Kans MDR1-MDCK
30.55	Pham The, H., González-/	9.5	http://www.cypro MDR1-MDCK
87	Pham The, H., González-/	9.92	Varma MV, Gardner MDR1-MDCK
12.30	Pham The, H., González-/	10.3	Wager , TT., Chandr MDR1-MDCK
5.47	Skolnik S, Lin X, Wang J.,	10.58	Varma MV, Sateesh MDR1-MDCK
14.5	Gertz M, Harrison A, Hou	10.7	Varma MV, Gardner MDCK II
7.72	Skolnik S, Lin X, Wang J.,	11.43	Varma MV, Sateesh MDCK II
16.15	Tacke R, Popp F, Müller E	12.3	Feng B, Mills JB, Dav MDCK II
22.81	Pham The, H., González-/	13.9	Gertz M, Harrison A MDR1-MDCK
20.33	Pham The, H., González-/	14.14	Varma MV, Gardner MDCK II
1.07	Sherer, EC., Verras, A., M	14.4	Varma MV, Gardner MDCK II
11.3	Dilger K, Schwab M, Fron	14.9	Varma MV, Gardner MDCK II
25.4	Jung SJ, Choi SO, Um SY.,	15	Varma MV, Gardner MDCK II
14	http://www.acrossbarrie	15.1	Wager , TT., Chandr MDR1-MDCK I
6.13	Pham The, H., González-/	16	Irvine JD, Takahashi MDCK (Strain
9.9	Bu HZ, Poglod M, Micetic	16	Huang L, Berry L, Ga MDCK (Strain
2.36	Laitinen L, Kangas H, Kau	16.1	Feng B, Mills JB, Dav MDCK II
11.80	Pham The, H., González-/	17.1	Varma MV, Sateesh MDR1-MDCK
45.36	Sherer, EC., Verras, A., M	17.1	Varma MV, Gardner MDCK II
22.30	Pham The, H., González-/	17.7	Feng B, Mills JB, Dav MDCK (strain

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16.20	Pham The, H., González-/	18.3	Varma MV, Gardner MDCK II
7	Crivori , P., Reinach, B. , F	18.4	Varma MV, Sateesh MDR1-MDCK
10.00	Pham The, H., González-/	18.67	Mashayekhi SO, Sat MDR1-MDCK
8.71	Pham The, H., González-/	19	Irvine JD, Takahashi MDCK II/ MDC
2.11	Saitoh R, Sugano K, Takat	19.4	Varma MV, Sateesh MDR1-MDCK
24.2	Gertz M, Harrison A, Hou	19.7	Feng B, Mills JB, Davidson RE,., et a
16.17	Pham The, H., González-/	20	Irvine JD, Takahashi MDCK (Strain
284.79	Sherer, EC., Verras, A., M	20.2	Varma MV, Gardner MDCK II
10.20	Pham The, H., González-/	22.5	Varma MV, Gardner MDCK II
12.7	Faassen F, Vogel G, Span	23.2	Wager , TT., Chandr MDR1-MDCK
31.9	Gertz M, Harrison A, Hou	23.4	Feng B, Mills JB, Dav MDCK (strain
58.70	Pham The, H., González-/	23.4	Varma MV, Gardner MDCK II
78.30	Pham The, H., González-/	23.4	Varma MV, Gardner MDCK II
17.74	Skolnik S, Lin X, Wang J.,	24.3	Varma MV, Gardner MDR1-MDCK
29.10	Pham The, H., González-/	24.7	Wager , TT., Chandr MDR1-MDCK
31.1	Crivori , P., Reinach, B. , F	24.8	Varma MV, Gardner MDCK II
21.9	Gertz M, Harrison A, Hou	25.9	Gertz M, Harrison A MDR1-MDCK (
19.63	Pham The, H., González-/	26.2	Irvine JD, Takahashi MDCK II/ MDC
1.48	Choi MK, Song IS., J Pharı	26.2	Gertz M, Harrison A MDR1-MDCK
48	Khan MZ, Rausl D, Zanosl	26.4	Varma MV, Sateesh MDR1-MDCK
21.6	Zerrouk N, Corti G, Ancill	27.1	Varma MV, Gardner MDCK II
20.10	Pham The, H., González-/	27.4	Varma MV, Gardner MDCK II
39.79	Skolnik S, Lin X, Wang J.,	27.5	Wager , TT., Chandr MDR1-MDCK
31.07	Skolnik S, Lin X, Wang J.,	28	Varma MV, Gardner MDCK II
8.65	Pham The, H., González-/	28.1	Varma MV, Gardner MDR1-MDCK
24.1	Gertz M, Harrison A, Hou	28.2	Gertz M, Harrison A MDR1-MDCK
17.7	Hassan HE, Myers AL, Lee	28.3	Wager , TT., Chandr MDR1-MDCK
29.55	Pham The, H., González-/	28.6	Wager , TT., Chandr MDR1-MDCK
40.00	Pham The, H., González-/	30.2	Luo S, Pal D, Shah SJ MDR1-MDCK
4.47	Sugawara M in the prese	30.8	Varma MV, Sateesh MDR1-MDCK
52.44	Pham The, H., González-/	30.8	Varma MV, Sateesh MDR1-MDCK I
19.42	Sherer, EC., Verras, A., M	31	Irvine JD, Takahashi MDCK (Strain
45.165	Yazdanian, M., Glynn, SL.	31.2	Varma MV, Gardner MDR1-MDCK
18.40	Pham The, H., González-/	31.4	Varma MV, Gardner MDCK II
52.48	Sherer, EC., Verras, A., M	32.7	Huang L, Berry L, Ga MDCK (Strain
25.4	Gertz M, Harrison A, Hou	34.6	Gertz M, Harrison A MDR1-MDCK I
28	Gertz M, Harrison A, Hou	35	Gertz M, Harrison A MDR1-MDCK
36.31	Sherer, EC., Verras, A., M	35	Chen LL, Yao J, Yang MDCK II
42	Pham The, H., González-/	35.2	Varma MV, Gardner MDCK II
67.01	Pham The, H., González-/	36	Varma MV, Gardner MDCK II
33.4	Yazdanian M, Briggs K, Ja	36.4	Varma MV, Gardner MDCK II
39.93	Pham The, H., González-/	36.63	Varma MV, Gardner MDR1-MDCK
119.00	Pham The, H., González-/	36.9	Gertz M, Harrison A MDR1-MDCK
149.32	Sherer, EC., Verras, A., M	37.6	Gertz M, Harrison A MDR1-MDCK (
15.1	Kanaan M, Daali Y, Dayer	40.2	Varma MV, Sateesh MDR1-MDCK I
22	Lennernäs H., Curr Drug I	42.7	Varma MV, Sateesh MDR1-MDCK
167.67	Pham The, H., González-/	43	Varma MV, Sateesh MDR1-MDCK
16	Teksin, ZS., Seo, PR., Polli	43.73333333	Varma MV, Gardner MDR1-MDCK
8.48	Marasanapalle VP, Crisor	43.8	Varma MV, Sateesh MDR1-MDCK
21.29	Skolnik S, Lin X, Wang J.,	44.95	Varma MV, Sateesh MDR1-MDCK
33.95	Pham The, H., González-/	45.25	Irvine JD, Takahashi MDCK II/ MDC
44.63	Pham The, H., González-/	46.1	Varma MV, Sateesh MDR1-MDCK
37.16	Sherer, EC., Verras, A., M	46.8	Varma MV, Gardner MDR1-MDCK
41.75	Skolnik S, Lin X, Wang J.,	49.45	Varma MV, Gardner MDR1-MDCK
26.70	Pham The, H., González-/	49.5	Varma MV, Sateesh MDR1-MDCK
22.68	Skolnik S, Lin X, Wang J.,	50.3	Varma MV, Sateesh MDR1-MDCK
43.55	Pham The, H., González-/	52.67	Varma MV, Gardner MDR1-MDCK
32.70	Pham The, H., González-/	52.9	Varma MV, Sateesh MDR1-MDCK
20.04	Pham The, H., González-/	55	http://www.hamilto Strian not stat

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25.88	Pham The, H., González-/	55.1	Varma MV, Sateesh MDR1-MDCK
42.32	Yamashita S, Furubayash	55.15	Varma MV, Gardner MDR1-MDCK
33.13	Pham The, H., González-/	59	Irvine JD, Takahashi MDCK (Strain
43.31	Pham The, H., González-/	59.8	Varma MV, Sateesh MDR1-MDCK
16.98	Pham The, H., González-/	60.4	Varma MV, Sateesh MDR1-MDCK I
6.90	Pham The, H., González-/	61.4	Varma MV, Sateesh MDR1-MDCK I
61.66	Pham The, H., González-/	65.1	Varma MV, Gardner MDR1-MDCK
30.33	Pham The, H., González-/	66.4	Varma MV, Gardner MDCK II
47.40	Pham The, H., González-/	69.9	Varma MV, Gardner MDCK II
52.00	Pham The, H., González-/	74.95	Varma MV, Gardner MDR1-MDCK
110.00	Pham The, H., González-/	88	Irvine JD, Takahashi MDCK (Strain
110.00	Pham The, H., González-/	110	Irvine JD, Takahashi MDCK (Strain
100	Irvine JD, Takahashi L, Lo	115.8	Irvine JD, Takahashi MDCK II/ MDC
150.00	Pham The, H., González-/	130	Irvine JD, Takahashi MDCK (Strain
43.90	Pham The, H., González-/	140	Irvine JD, Takahashi MDCK (Strain
89.3	Saitoh R, Sugano K, Takat	160	Irvine JD, Takahashi MDCK (Strain
1.50	Pham The, H., González-/	166.8	Varma MV, Gardner MDCK II

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Experimental Solubility mg/ml	*Solubility Reference*	*Comments e.g conditio -pH, (temp in ^{o} C)*	*Maximum Strength Dose*	*Maximum Strength Dose UNITS*	*Maximum Strength Reference*	*Maximum Strength Comments*
0.0000115	AQUASOL dATAbASI	25	1000	mg	British Natior	Tablet (AS SOD
II			500	mg	FDA Orange E	Capsule (AS HY
II			1500	mg	British Natior	Solution (IV INF
0.24	Hazardous Substanc	pH1.8	500	mg	British Natior	Tablet as potas
II			8	mg	British Natior	Capsule (AS HY
II			2	mg/ml	British Natior	Solution (AS HY
>0.0622	Pubchem (AID 1996	pH 7.4 (22.5-24.5)	50	mg/ml	Benet LZ, Bro	Solution (IV AS
4	AQUASOL dATAbASE	6th edition	1000	mg	British Natior	Tablet
II			2.5	mg	British Natior	Tablet
1.817	AQUASOL dATAbASI	25	800	mg	British Natior	Tablet
			320	mg	British Natior	Tablet (AS HYD
70	AQUASOL dATAbASI	RT	300	mg	British Natior	Tablet
(strain not stated)			400	mg	British Natior	Tablet
97	The Merck Index: 12th edition 1996		80	mg	British Natior	Tablet (AS DIHY
(strain not stated)			75	mg	British Natior	Capsule (AS PH
not stated)			800	mg	British Natior	Tablet
0.055	AQUASOL dATAbASI	mesylate (25)	1000	mg	British Natior	Tablet (AS MES
			800	mg	British Natior	Tablet
3.37	AQUASOL dATAbASI	25	500	mg	British Natior	Solution (IV INF
0.01	AQUASOL dATAbASE	6th edition	2000	mg	FDA Orange E	Tablet
0.08499	AQUASOL dATAbASI	25	320	mg	British Natior	Tablet
9.3	AQUASOL dATAbASI	Intrinsic (25)	800	mg	British Natior	Tablet
101	Balaguer-Fernández	succinate salt (20)	100	mg	British Natior	Tablet (AS SUC
1000	AQUASOL dATAbASE	6th edition	2.5	mg/ml	British Natior	Solution (IV INJ
550	Kortejarvi, H., Ylipe	pH 1–7.4, Hydrochl	300	mg	British Natior	Tablet (AS HYD
<0.003	Oh YK, Nix DE, Straubinger RM., Antimic		1000	mg	British Natior	Tablet (AS MOI
0.0011	AQUASOL dATAbASI	25	40	mg	British Natior	Tablet
			500	mg	British Natior	Capsule
0.44	AQUASOL dATAbASI	25	500	mg	British Natior	Tablet (Coated
0.2827	AQUASOL dATAbASI	25	500	mg	FDA Orange E	Tablet
:K (strain not stated)						
(strain not stated)			40	mg	British Natior	Tablet (AS CAL
0.528	AQUASOL dATAbASI	dihydrate (30)	500	mg	British Natior	Tablet
4.549	AQUASOL dATAbASI	25	20	mg	British Natior	Tablet
0.0062	AQUASOL dATAbASI	25	80	mg	FDA Orange E	Tablet
0.02	Ghai D, Sinha VR., Nanomedicine. 2012 .		100	mg	Krueger M, A	Tablet
not stated)			400	mg	Martindale, T	Capsule
0.605	AQUASOL dATAbASI	25	50	mg	British Natior	Tablet (Coadmi
209.2	AQUASOL dATAbASE	6th edition	40	mg	FDA Orange E	Powder (inhala
II			1	mg/ml	British Natior	Solution (IV INJ
90	Reverchon E, Della Porta G., Int J Pharm		5	mg	British Natior	Tablet (AS SULF
(strain not stated)			400	mg	British Natior	Tablet
0.0135	AQUASOL dATAbASI	Intrinsic (25)	100	mg	British Natior	Tablet
10	AQUASOL dATAbASI	25	500	mg	British Natior	Tablet (anhydr
0.00045	AQUASOL dATAbASI	22.5	50	mg	British Natior	Tablet
II/ MDCK (strain not stated)			400	mg	Hunt D, McRa	Tablet
II/ MDCKII			30	mg	British Natior	Tablet
0.086	AQUASOL dATAbASI	25	750	mg	British Natior	Tablet (AS HYD
not stated)			200	mg	Fillastre JP, G	Tablet
II			50	mg	British Natior	Powder (IV INJI

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8.3	AQUASOL dATAbASI	25	240	mg	British Natior Tablet
0.0464	AQUASOL dATAbASI	25	0.25	mg	British Natior Tablet
0.711	Hopfinger AJ, Esposi	Intrinsic	400	mg	British Natior Capsule as hyd
			150	mg	British Natior Tablet (AS POT
1087	AQUASOL dATAbASI	25	200	mg	British Natior Capsule (AS HY
0.0171	AQUASOL dATAbASI	pH 6.5 (22)	20	mg	British Natior Tablet (AS MAL
4.24	Deák K, Takács-Novák K, Tihanyi K, et al.		50	mg	Martindale, T Tablet (AS HYD
			500	mg	FDA Orange E Capsule (AS SO
0.1145	AQUASOL dATAbASI	25	200	mg	British Natior Capsule 1.9m^
0.7	Gu X, Li H, Macnair I	pH 6.8, 25	8	mg	British Natior Capsule
0.00617	AQUASOL dATAbASI	22.5	300	mg	British Natior Capsule
0.04	Cao, D., Wang, J., Zh	25	600	mg	http://www.a Capsule
21	AQUASOL dATAbASI	Maleate (25)	40	mg	British Natior Tablet (AS MAL
			500	mg	British Natior Tablet
II/MDCKII			10	mg	FDA Orange E Tablet (AS HYD
2.2	SRC PHYSPROP		50	mg	British Natior Tablet
0.00346	Hopfinger AJ, Esposi	Intrinsic	150	mg	British Natior Tablet
3.19	AQUASOL dATAbASI	25	1750	mg	British Natior Capsule (25mg,
(strain not stated)			200	mg	British Natior Tablet (AS ACE
0.0097	SRC PHYSPROP	24	200	mg	British Natior Tablet (AS HYD
not stated)			250	mg	British Natior Tablet (AS MOI
4.5	AQUASOL dATAbASE	6th edition	1250	mg	British Natior Tablet (AS MES
659	AQUASOL dATAbASI	25	10	mg	British Natior Tablet (AS HYD
4.62	AQUASOL dATAbASI	25	750	mg	FDA Orange E Capsule
ferent concentration, MDCK wild type used			250	mg	http://www.a Capsule
0.01	AQUASOL dATAbASI	ambient temp	400	mg	British Natior Tablet
2.75	Ross, DL., Riley, CM.	Intrinsic (25)	400	mg	British Natior Tablet
50	http://www.sigmaa	Diphosphate salt in	310	mg	British Natior Tablet as base
0.01	AQUASOL dATAbASE	6th edition	600	mg	British Natior Tablet
14	http://www.accessc	Hydrochloride salt	60	mg	British Natior Capsule (AS HY
0.19	AQUASOL dATAbASE	6th edition	600	mg	British Natior Capsule
0.212	AQUASOL dATAbASI	25	5	mg	FDA Orange E Tablet
0.00633	AQUASOL dATAbASI	25	5	mg	FDA Orange E Tablet (AS ACE
20.1	SRC PHYSPROP	25	300	mg	British Natior Capsule
0.00122	AQUASOL dATAbASI	25	0.10	%	British Natior Topical (AS MC
3.322	AQUASOL dATAbASI	25	0.6	mg/ml	British Natior Solution (IV INJ
0.0113	SRC PHYSPROP		0.5	mg	FDA Orange E Tablet
0.1889	Hopfinger AJ, Esposi	Intrinsic	200	mg	British Natior Tablet
0.009319	AQUASOL dATAbASI	pH 8.2 (25)	40	mg	FDA Orange E Tablet
249	AQUASOL dATAbASI	25	2000	mg	Levine GN, Fr Tablet
1	AQUASOL dATAbASE	6th edition	800	mg	British Natior Capsule
0.403	AQUASOL dATAbASI	25	200	mg	British Natior Tablet
0.0004336	Alelyunas YW, Liu R,	pH7.4	80	mg	FDA Orange E Capsule
0.0000001	AQUASOL dATAbASI	25	120	mg	Martindale, T Tablet
0.0004	Hazardous Substances Data Bank (HSDB		80	mg	FDA Orange E Tablet
0.0032	AQUASOL dATAbASI	22.5	5	mg	British Natior Tablet (AS HYD
0.002058	AQUASOL dATAbASI	22.5	20	mg	British Natior Tablet
0.00453	AQUASOL dATAbASI	22	10	mg	British Natior Tablet
0.14	AQUASOL dATAbASI	25	400	mg	FDA Orange E Tablet (AS SULI
0.00145	Llinàs A, Glen RC, Gc	Intrinsic (25)	15	mg	British Natior Tablet
0.115	AQUASOL dATAbASI	25	20	mg	British Natior Tablet
			40	mg	British Natior Capsule (AS SO
(strain not stated)			40	mg	British Natior Tablet (AS HYD
0.539	AQUASOL dATAbASI	25	100	mg	British Natior Tablet
0.0007599	AQUASOL dATAbASI	22.5	300	mg	British Natior Tablet (AS HYD
			25	mg	British Natior Tablet (AS HYD
100	AQUASOL dATAbASE	6th edition	0.3	mg	British Natior Tablet (Chewat
7.55	AQUASOL dATAbASI	25	500	mg	British Natior Tablet (Modifie
0.2	SRC PHYSPROP	25	20	mg	British Natior Tablet

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0.01823	AQUASOL dATAbASE	24		150	mg	British Natior Tablet (S HYDR
0.321	AQUASOL dATAbASE	pH 5.8 (30)		10	mg	Lefebvre RA, Tablet
0.345	AQUASOL dATAbASE	25		50	mg	British Natior Tablet (AS SULI
0.117	SRC PHYSPROP	25		400	mg	British Natior Tablet (AS HYD
0.00207	AQUASOL dATAbASE	6th edition		4.8	mg	http://www.a Capsule (AS MI
0.127	Hopfinger AJ, Esposi	Intrinsic		400	mg	British Natior Tablet (AS HYD
0.0985	AQUASOL dATAbASE	25		2	mg	British Natior Tablet
0.0137	Llinàs A, Glen RC, Gc		25	200	mg	FDA Orange E Tablet (co-adm
52.3	AQUASOL dATAbASE	25		1	mg/ml	British Natior Solution (IM)
0.04474	AQUASOL dATAbASE	25		6	mg	British Natior Tablet
<0.01	AQUASOL dATAbASE	Tartrate (25)		10	mg	British Natior Tablet (AS TAR
0.0035	AQUASOL dATAbASE	32		50	mg	British Natior Tablet (AS SOD
				60	mg	British Natior Capsule
43	AQUASOL dATAbASE	tartrate (25)		200	mg	British Natior Tablet (AS TAR
0.054	AQUASOL dATAbASE	6th edition		2.5	mg	British Natior Tablet
0.0388	AQUASOL dATAbASE	25 (different polym		100	mg	British Natior Tablet (chewat
(strain not stated)				10	mg	British Natior Tablet (AS HYD
0.051	AQUASOL dATAbASE	25		100	mg	British Natior Capsule
3.488	AQUASOL dATAbASE	citrate		100	mg	British Natior Tablet (AS CITR
0.01	Janssens F, Leenaerts J, Diels G., et al., J			10	mg	British Natior Tablet
0.031	AQUASOL dATAbASE	25		10	mg	Martindale, T Tablet
0.0325	AQUASOL dATAbASE	25		100	mg	British Natior Tablet
0.17	Benet LZ, Broccatelli	F, Oprea TI., AAPS J		3	mg	Oda M, Kotej Tablet
0.0159	AQUASOL dATAbASE	25		500	mg	British Natior Tablet
0.0025500	SRC PHYSPROP	24		100	mg	British Natior Tablet (AS HYD
0.08999	AQUASOL dATAbASE	25		4	mg	British Natior Tablet
142.9	AQUASOL dATAbASE	hydrochloride salt		20	mg	British Natior Capsule (AS HY
0.014	AQUASOL dATAbASE	pH 1-7 (25)		300	mg	British Natior Capsule (AS SO
0.007	DeGoey DA, Grampovnik DJ, Flosi WJ., e			800	mg	British Natior Tablet (WITH R
11.05	AQUASOL dATAbASE	Maleate (37.5)		45.3	mg	http://www.r Tablet
II				160	mg	British Natior Tablet (AS HYD
0.33	AQUASOL dATAbASE	25		20	mg	British Natior Tablet
21.6	AQUASOL dATAbASE	25		200	mg	FDA Orange E Tablet
0.0061860	AQUASOL dATAbASE	pH 2 (24.9)		500	mg	FDA Orange E Tablet
0.125	AQUASOL dATAbASE	24		2000	mg	British Natior Tablet
II, MDCKII, MDCK-MDR1 (strain not stated)				10	mg	British Natior Tablet (AS HYD
0.03	AQUASOL dATAbASE	ambient temp		0.5	mg	FDA Orange E Tablet
14.475	AQUASOL dATAbASE	25		1000	mg	British Natior Tablet
0.0138	AQUASOL dATAbASE	25		800	mg	British Natior Tablet
0.0468	AQUASOL dATAbASE	25		15	mg	British Natior Tablet
0.004	AQUASOL dATAbASE	37		1200	mg	FDA Orange E Tablet
0.51	AQUASOL dATAbASE	hydrochloride salt (		300	mg	British Natior Capsule (modif
0.07	AQUASOL dATAbASE	ambient temp		500	mg	British Natior Tablet
(strain not stated)				5	mg/ml	British Natior Solution (IV AS
II				150	mg	British Natior Tablet (AS HYD
2.119	Sköld C, Winiwarter	Intrinsic		100	mg	British Natior Capsule
0.01564	AQUASOL dATAbASE	24		25	mg	British Natior Tablet (AS HYD
5.496	AQUASOL dATAbASE	37.5		4	mg	British Natior Tablet (AS MAL
0.92	Lee J, Park TG, Choi	Hydrochloride		40	mg	FDA Orange E Capsule
0.08099	AQUASOL dATAbASE	25		160	mg	British Natior Tablet (AS HYD
0.017	SRC PHYSPROP	20		10	mg	British Natior Tablet (AS SOD
0.3669	AQUASOL dATAbASE	22.5		200	mg	Benet LZ, Bro Tablet
0.41	Hopfinger AJ, Esposi	Intrinsic (25)		50	mg	British Natior Capsule
0.15	AQUASOL dATAbASE	25		400	mg	British Natior Tablet
0.414	Llinàs A, Glen RC, Gc	Intrinsic (25)		1	mg/ml	British Natior Solution (IV)
0.7205	Bergström CA, Luthman K, Artursson P.,			240	mg	British Natior Tablet (AS HYD
0.054	AQUASOL dATAbASE	24		5	mg/ml	British Natior Solution (IV AS
182.767	Bergström CA, Wass	hydrochloride salt		0.075	mg	British Natior Tablet (AS HYD
ed				30	mg	British Natior Tablet (AS MAL

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0.0586	SRC PHYSPROP	24	300	mg	FDA Orange E	Tablet (AS HYD
637	AQUASOL dATAbASI	25	500	mg	Benet LZ, Bro	Tablet
0.033	AQUASOL dATAbASI	22.5	15	mg	British Natior	Tablet
11	Hazardous Substanc	Acetate (25)	32	mg	Martindale, T	Tablet
ll			20	mg	Martindale, T	Tablet
ll			40	mg	British Natior	Capsule (AS HY
3.85	AQUASOL dATAbASI	25	100	mg	British Natior	Solution (IV INJ
0.084	AQUASOL dATAbASI	25	20	mg	British Natior	Tablet
0.1	Gao S, Singh J., J. Control Release, 1998,		80	mg	British Natior	Tablet (AS CITR
0.0058	AQUASOL dATAbASI	25	20	mg	British Natior	Capsule
0.17	http://www.accessc	25	100	mg	British Natior	Tablet
0.035208	Alelyunas YW, Liu R,	pH 7.4	8	mg	British Natior	Tablet (AS HYD
0.0279	AQUASOL dATAbASI	25	40	mg	British Natior	Capsule (AS UN
78.7	Alelyunas YW, Empfield JR, McCarthy D.		150	mg	British Natior	Tablet
0.2405	AQUASOL dATAbASI	37				
0.0089	AQUASOL dATAbASI	25	100	mg	British Natior	Capsule (Micro
3.79	AQUASOL dATAbASI	25	200	mg	British Natior	Capsule (Co ad
			70	mg	British Natior	Tablet (AS SOD
12	SRC PHYSPROP	20	2000	mg	British Natior	Powder (IV INF
85			1600	mg	British Natior	Capsule (AS SO
85			25	mg	FDA Orange E	Tablet (AS CAL(
0.119	www.toku-e.com/ConvertHtmlToPdf.ax		40000	mg	FDA Orange E	Powder (IV INJE
85			24	mg/ml	British Natior	Solution (IV INF
229.8	AQUASOL dATAbASI	25				
0.005	US Patent 2006/0073200 A1, Serial num		20	mg	British Natior	Tablet (AS HYD
85			2000	mg	Ko H, Cathca	Solution (IV AS
85			3	mg	Evans HC, Pe	Powder (SC)
13	AQUASOL dATAbASI	25	24	mg	Martindale, T	Tablet
0.75	AQUASOL dATAbASI	28	100	mg	Martindale, T	Powder (IV INJE
2.76	Thomas S, Brightma	pH 7.4, Hydrochlori	40	mg	http://www.a	Tablet (AS HYD
85			5	mg	Dudenhauser	Tablet
>100	Hazardous Substanc	20	200	mg	Martindale, T	Capsule
85			4000	mg	British Natior	Solution (IV INF
85			20	mg	FDA Orange E	Tablet (AS SULF
500	http://www.accessc	Chloride	20	mg	British Natior	Tablet (AS CHL(
0.5135	AQUASOL dATAbASE	6th edition	187.4	mg/ml	FDA Orange E	Solution (IV)
142	Hazardous Substanc	25	600	mg	British Natior	Tablet
85			200	mg	Bastain W, B(	Tablet
0.8	SRC PHYSPROP	25	10	mg	British Natior	Tablet (AS HYD
0.7112	AQUASOL dATAbASI	25	500	mg	British Natior	Tablet/Capsule
27.3	AQUASOL dATAbASI	25	400	mg	British Natior	Capsule (granul
764	SRC PHYSPROP	30	20000	mg	FDA Orange E	Powder (ORAL)
1.41	French, DL., Mauger	37	4800	mg	British Natior	Tablet
			400	mg	FDA Orange E	Tablet
'6-81						
0.0029	AQUASOL dATAbASI	30	20	mg	British Natior	Tablet
			2000	mg	British Natior	Solution (IV INJ
			500	mg	FDA Orange E	Powder (IV INJE
16	Kurochkina VB, Skly	For propylene glycc	500	mg	Mastrandrea	Capsule
85			50	mg	Martindale, T	Tablet (AS HYD
13.9	AQUASOL dATAbASI	25	1000	mg	British Natior	Capsule
0.004	AQUASOL dATAbASE	6th edition	12	mg	FDA Orange E	Tablet
85			400	mg	FDA Orange E	Capsule
0.04	AQUASOL dATAbASI	25	1000	mg	British Natior	Capsule
167	SRC PHYSPROP		1500	mg	British Natior	Tablet
85			20	mg	FDA Orange E	Tablet (AS BRO
85			300	mg	British Natior	Powder (IV AS I
85			2000	mg	British Natior	Solution (IV AS

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85			300	mg	British Natior Tablet
56			666	mg	British Natior Tablet (AS CALC
			200	mg	British Natior Tablet
	80.1	AQUASOL dATAbASI 16			
	32.1	US Patent 2005/0171,203 Serial numbe	300	mg	British Natior Tablet
	4.5	http://www.accessc 24	400	mg	http://www.accessdata.fda.g
			200	mg	British Natior Tablet
85			850	mg	British Natior Tablet (AS HYD
	0.1083	AQUASOL dATAbASI 25	10	mg	Benet LZ, Bro Tablet (Co-adm
			10	mg	FDA Orange E Tablet (active n
	0.529	AQUASOL dATAbASI 20	1000	mg	FDA Orange E Tablet
	>50	He H, Tran P, Yin H., Unpublished results	50	mg	British Natior Tablet
	10	AQUASOL dATAbASE 6th edition	500	mg	British Natior Capsule (AS MC
	2.675	AQUASOL dATAbASI 25	2400	mg	British Natior Powder (IV INJE
			4000	mg	British Natior Powder (IV INJE
			40	mg	British Natior Tablet (AS SOD
	0.0016	AQUASOL dATAbASI 25	5	mg	British Natior Tablet
			0.5	mg/ml	British Natior Solution (IV AS
	<0.01	AQUASOL dATAbASI RT	10	mg	British Natior Tablet (AS MAL
	0.00532	Kumar, N., Jain, AK., Hydrochloride (27)	250	mg	British Natior Tablet (AS HYD
			20	mg	FDA Orange E Tablet (AS HYD
	21.3	AQUASOL dATAbASE 6th edition	500	mg	FDA Orange E Capsule
	5	Chen XQ, Cho SJ, Li Y., et al., J Pharm Sci	3000	mg	British Natior Powder for IV r
			10000	mg	FDA Orange E Solution (IV INJ
	0.00025	Hazardous Substances Data Bank (HSDB	60	mg	British Natior Tablet (AS HYD
	174	http://www.fda.gov Hydrochloride	1000	mg	British Natior Tablet
			0.024	mg	British Natior Powder for inh
	0.19	AQUASOL dATAbASI 25	400	mg	British Natior Tablet
	0.0339	Pubchem (AID 1996 pH 7.4 (22.5-24.5)	200	mg	Ballerini R, Ca Capsule
			100	mg	Smith, PC., M Tablet (AS dihy
	4.46	AQUASOL dATAbASI 25 (different forms	900	mg	British Natior Tablet
	0.0428	Sköld C, Winiwarter S, Wernevik J., et al	0.2	mg	British Natior Tablet
			10000	mg	FDA Orange E Solution (IV INJ
	0.09948	AQUASOL dATAbASI EFG (20)	500	mg	British Natior Tablet
	1.03	Ross, DL., Riley, CM. Intrinsic (25)	400	mg	FDA Orange E Tablet
PharmR.pdf			1000	mg	British Natior Tablet
	2.792	AQUASOL dATAbASI pH 7.5 (RT)	300	mg	FDA Orange E Capsule
			150	mg	Kanamitsu SI, Tablet
	0.01	AQUASOL dATAbASE 6th edition	1.5	mg	FDA Orange E Tablet
	0.183	AQUASOL dATAbASI 32	10	mg	British Natior Tablet
	94.6	http://www.fda.gov/downloads/Drugs/	5	mg	British Natior Tablet
	0.457	Llinàs A, Glen RC, Gc Intrinsic (25)	1000	mg	FDA Orange E Solution (IV INF
	85	AQUASOL dATAbASI 24.8	40	mg	British Natior Capsule
			250	mg	Welker HA., J Tablet
PharmR.pdf			25	mg	British Natior Tablet (AS HYD
	0.0603	AQUASOL dATAbASI 25	5	mg	British Natior Tablet
BioPharmr.pdf			90	mg	British Natior Tablet (AS HYD
	0.383	Ross, DL., Riley, CM. Intrinsic (25)	400	mg	FDA Orange E Tablet
	0.007	AQUASOL dATAbASI 37	200	mg	British Natior Tablet
ug;370(2):124-30			0.8	mg	http://www.a Tablet (AS SOD
	0.01	AQUASOL dATAbASE 6th edition	400	mg	http://www.a Tablet
	0.74	Harrison A, Betts A, Fenner K, et al, Drug Metab Dispos, 2004, 32,197-204.			
			600	mg	British Natior Tablet
	0.533	Tolle-Sander S, Grill pH 7.5	200	mg	Roy P, Jakate Tablet
	0.0721	AQUASOL dATAbASI 25	1000	mg	British Natior Tablet
here ph gradient (6 to 7.4 from A-B sides taken)					
71			0.004	mg	FDA Orange E Capsule

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:372-80			20	mg	British Natior Tablet
0.0306	AQUASOL dATAbASI	22.5	10	mg	British Natior Tablet (AS HYD
0.08468	AQUASOL dATAbASI	25	4	mg	British Natior Tablet
0.02	AQUASOL dATAbASI	37	600	mg	FDA Orange E Tablet
			1000	mg	British Natior Capsule
			100	mg	FDA Orange E Tablet (AS HYD
0.02153	AQUASOL dATAbASE	6th edition	3	mg	Benet LZ, Bro Capsule
~0.0015	http://www.accessdata.fda.gov/drugsat		800	mg	British Natior Capsules
			1	mg/ml	British Natior OPHTHALMIC (
0.034	AQUASOL dATAbASI	25	200	mg	FDA Orange E Tablet/Capsule
0.001801	AQUASOL dATAbASI	22.5	100	mg	British Natior Tablet (AS HYD
0.0176	Srivijaya,R., Vishweshwar, P., Sreekanth,		6	mg	FDA Orange E Tablet
0.15	AQUASOL dATAbASI	pH 7.4 (25)	100	mg	British Natior Tablet
0.1	AQUASOL dATAbASI	37	600	mg	British Natior Tablet (AS CALC
			300	mg	British Natior Tablet
0.35	http://www.accessc	pH 7 (37)	320	mg	FDA Orange E Tablet
0.292	AQUASOL dATAbASI	37	1000	mg	Martindale, T Tablet
0.0213	AQUASOL dATAbASI	25	200	mg	British Natior Tablet
85			750	mg	Massarella JV Capsule
			300	mg	British Natior Tablet (AS BISU
			200	mg	FDA Orange E Tablet (AS MES
1			2	mg	British Natior Tablet (AS DIHY
12			150	mg	FDA Orange E Tablet (AS CITR
0.4383	AQUASOL dATAbASI	25	2000	mg	FDA Orange E Tablet
2.18	AQUASOL dATAbASI	25	tive metabolite		
0.007	AQUASOL dATAbASI	25	400	mg	British Natior Capsules
0.0048	AQUASOL dATAbASI	22.5	50	mg	British Natior Tablet (AS HYD
280	Llinàs A, Glen RC, Gc	Intrinsic (25)	300	mg	FDA Orange E Tablet
85			10	mg	Sloan TP, Ma Tablet (AS SULF
119.0	AQUASOL dATAbASE	6th edition	50	mg	British Natior Tablet
0.691	Ross, DL., Riley, CM.	Intrinsic (25)	400	mg	Naber KG, Th Tablet
transporters.			0.5	mg	FDA Orange E Capsule
0.0000055	AQUASOL dATAbASI	100	10	mg	British Natior Tablet
85			500	mg	FDA Orange E Capsule
85			80	mg	British Natior Tablet
0.16	AQUASOL dATAbASI	ambient temp	20	mg/ml	British Natior Emulson (IV INJ
>0.0281	Pubchem (AID 1996	pH 7.4 (22.5-24.5)	75	mg	Park GB, Kers Capsule no long
0.012	AQUASOL dATAbASI	25	15	mg	British Natior Tablet
0.02	SRC PHYSPROP	30	500	mg	British Natior Tablet
85			12	mg	FDA Orange E Tablet (AS MAL
			15	mg	British Natior Tablet
450.5	AQUASOL dATAbASI	25	100	mg/ml	FDA Orange E Solution (IV)
PharmR.pdf			0.3	mg	British Natior Inhalation pow
0.000101	Patel, SG., and Rajpu	37	100	mg	British Natior Tablet
27	AQUASOL dATAbASI	25	500	mg	Martindale, T Tablet
e 2, pp 177-186			0.075	mg	Martindale, T Tablet (co-adm
2.7	http://www.accessdata.fda.gov/drugsat		25	mg	FDA Orange E Tablet
0.265	AQUASOL dATAbASI	25	1000	mg	FDA Orange E Tablet
<0.005	Cao, D., Wang, J., Zhou, R. et al, J Chem		150	mg	British Natior Tablet
0.04	AQUASOL dATAbASI	37	600	mg	British Natior Tablets
0.009	AQUASOL dATAbASI	25	50	mg	FDA Orange E Tablet
1000	SRC PHYSPROP		4	mg	FDA Orange E INHALANT CAR
0.0619	AQUASOL dATAbASI	32	20	mg	British Natior Tablet
0.025	Grbic S, Parojcic J, Ib	pH 4.37	160	mg	British Natior Tablet
0.197	McGuirk PR, Jefson	pH 7.2	800	mg	Martindale, T Tablet
85			100	mg	British Natior Capsule (AS HY
il was calculated from the total concentrations of temocapril			10	mg	Püchler K, Sie Tablet
PharmR.pdf			10	mg	FDA Orange E Tablet
2.7	http://www.ema.eu	pH 1.2	400	mg	British Natior Tablet

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	0.05	Hazardous Substanc	20	500	mg	FDA Orange E Powder (IV)
	9.705	AQUASOL dATAbASE 6th edition		200	mg	British Natior Tablet
1				2000	mg	British Natior Tablet
	0.1708	AQUASOL dATAbASI	pH 7	400	mg	British Natior Tablet
	0.0123	SRC PHYSPROP	25	200	mg	FDA Orange E Tablet
	>0.0736	Pubchem (AID 1996	pH 7.4 (22.5-24.5)	6	mg	British Natior Tablet
	0.002	http://www.accessdata.fda.gov/drugsat		160	mg	http://www.a Capsule
	0.5497	AQUASOL dATAbASI	hydrochloride (25)	600	mg	British Natior Tablet (AS SULF
	<0.5	AQUASOL dATAbASI	RT	60	mg	British Natior Tablet (AS HYD
				30	mg	Ferrillo F, Bal Tablet
	0.03733	AQUASOL dATAbASI	37.5	600	mg	Martindale, T Capsule (AS HY
	50.3	AQUASOL dATAbASI	25	300	mg	Benet LZ, Bro Tablet
	0.01	SRC PHYSPROP	25	40	mg	Martindale, T Tablet
85						
				1000	mg	FDA Orange E Tablet
	<0.002	US Patent 2008/0171,013 A1 Serial num		40	mg/ml	British Natior Suspension
				10	mg	FDA Orange E Tablet (AS SULF
				300	mg	Martindale, T Tablet
				200	mg	Martindale, T Tablet
	0.15	AQUASOL dATAbASI	25	200	mg	The Treatme Tablet
	38.6	http://www.accessc	pH 6.99	20	mg	British Natior Tablet (AS HYD
85				20	mg	Benet LZ, Bro Tablet (AS HYD
	0.4	AQUASOL dATAbASE 6th edition		2400	mg	FDA Orange E Tablet
				60	mg	Martindale, T Tablet
85						
	~200	Hazardous Substances Data Bank (HSDB		60	mg	FDA Orange E Tablet
	1.65	AQUASOL dATAbASE 6th edition		500	mg	British Natior Tablet (AS SEM
85				120	mg	Coates PE, M Capsule (AS SO
	0.0767	Nayak, AM., and Par	RT	120	mg	British Natior Capsule
	218	AQUASOL dATAbASI	25	15	mg/ml	FDA Orange E Solution
	>0.0254	Pubchem (AID 1996	pH 7.4 (22.5-24.5)	750	mg	FDA Orange E Tablet
	0.1	Pilbrant, A., Cederberg, C., Scand J Gastr		60	mg	British Natior Capsule
	2.494	AQUASOL dATAbASI	25	10	mg	Merkel U, Sig Capsule
	10.69	AQUASOL dATAbASI	25	60	mg	British Natior Tablet (AS PHO
'				2	mg	Benet LZ, Bro Tablet (AS HYD
85				10	mg	British Natior Tablet
	1.204	AQUASOL dATAbASI	Intrinsic (25)	50	mg	British Natior Tablet
	>0.0406	Pubchem (AID 1996	pH 7.4 (22.5-24.5)	10	mg	Greenblatt D. Tablet
85				2	mg	British Natior Tablet (AS HYD
	0.035	AQUASOL dATAbASI	22	50	mg	British Natior Tablet
				400	mg	FDA Orange E Capsule (AS HY
ed				7000	mg	British Natior Tablet 200mg/
	649	Becker C, Dressman	dihydrochloride sal	400	mg	British Natior Tablet (AS HYD
	0.0026	Pubchem (AID 1996	25	6	mg	British Natior Tablet
	6.213	Kwon JW, Armbrust KL., Bull Environ Co		60	mg	British Natior Tablet (AS HYD
II				120	mg	British Natior Tablet (AS BRO
	0.049	Hazardous Substanc	Mesylate pH 7.4	400	mg	British Natior Tablet (AS MES
	0.0000017	AQUASOL dATAbASI	32	600	mg	British Natior Tablet (AS SULF
	52	AQUASOL dATAbASI	25	100	mg	British Natior Tablet
	20	Harnden MR, Jarvest RL, Boyd MR., et al		750	mg	British Natior Tablet
	0.124	AQUASOL dATAbASI	25	100	mg	British Natior Tablet
(strain not stated)				250	mg	British Natior Tablet (AS HYD
(strain not stated)				1	mg	British Natior Tablet (AS MES
	250	US Patent 2009/014	Mesylate	4	mg	British Natior Tablet (AS MES
	>10	US Patent 2010/008	pH 7.4	0.7	mg	British Natior Tablet
II				2	mg	Martindale, T Tablet
II				20	mg/ml	FDA Orange E Solution (IV AS
	0.004	Ghazal, H. S.; Dyas, A	pH 1	200	mg	British Natior Capsule (enclos
	0.0030546	Yu, J., He, H., Tang, X., J. Pharm. Pharma		60	mg	British Natior Tablet

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31	http://www.janssen	HBr salt	12	mg	British Natior Tablet (AS HYD
27.8	Cao, D., Wang, J., Zh	hydrochloride salt	120	mg	British Natior Capsule (AS HY
II			4	mg	British Natior Tablet (AS MAL
10.3	AQUASOL dATAbASI	25	500	mg	British Natior Tablet
(strain not stated)			20	mg	British Natior Tablet
(strain not stated)			15	mg	British Natior Tablet (AS HYD
<0.1	AQUASOL dATAbASI	RT	187.5	mg	British Natior Tablet (AS HYD
122.8	AQUASOL dATAbASI	25	100	mg	British Natior Tablet
2.37	http://www.medicir	Fumarate salt	400	mg	British Natior Tablet (AS FUM
0.0037	AQUASOL dATAbASI	hydrochloride, intri	100	mg	FDA Orange E Tablet (AS NAP
(strain not stated)			12.5	mg	http://www.s Tablet (AS SOD
(strain not stated)			45	mg	British Natior Tablet
190	AQUASOL dATAbASI	pH 3-7.9 (25)	750	mg	British Natior Capsule
133	http://www.accessc	Hydrochloride	8	mg	British Natior Tablet (AS HYD
(strain not stated)			6	mg	British Natior Tablet (AS HYD
(strain not stated)			50	mg	British Natior Tablet (AS HYD
0.8	http://www.accessdata.fda.gov/drugsat		200	mg	FDA Orange E Capsule
(strain not stated)			10	mg	FDA Orange E Tablet (AS BITA
(strain not stated)			50	mg	British Natior Tablet
0.02828	AQUASOL dATAbASI	24	8	mg	British Natior Tablet
0.1	SRC PHYSPROP	25	2	mg	British Natior Tablet
14.869	Henry TB, Kwon JW,	22	150	mg	British Natior Tablet (AS MAL
0.21	http://www.ema.europa.eu/docs/en_G		8	mg	FDA Orange E Tablet
0.025	Llinàs A, Glen RC, Gc	Intrinsic (25)	100	mg	British Natior Tablet (AS HYD
			8	mg	FDA Orange E Tablet
0.8	Miyamoto, E; Kawas	pH 6	5	mg	British Natior Tablet (AS HYD
(strain not stated)			300	mg	British Natior Tablet
II			150	mg	FDA Orange E Capsule (AS HY
(strain not stated)			10	mg	British Natior Tablet
0.043	AQUASOL dATAbASI	30	10	mg	British Natior Tablet
>0.5	AQUASOL dATAbASE	6th edition	600	mg	British Natior Tablet
0.0048	Llinàs A, Glen RC, Gc	Intrinsic (25)	75	mg	British Natior Capsule (AS MA
			100	mg	Amery WK, H Tablet
II			20	mg/ml	British Natior Solution (IV INJ
0.0008334	AQUASOL dATAbASI	22.5	75	mg	FDA Orange E Tablet (AS HYD
1.13	AQUASOL dATAbASI	25	180	mg	British Natior Tablet
0.03157	AQUASOL dATAbASI	25	100	mg	British Natior Capsule (AS HY
II			0.3	mg/ml	British Natior Solution (IV INJ
II			60	mg	Dayer P, Bala Tablet
0.001055	AQUASOL dATAbASI	22.5	30	mg	British Natior Tablet (AS HYD
II			10	mg	British Natior Tablet (AS HYD
500	Hazardous Substanc	Dihydrochloride sal	30	mg	British Natior Capsule (AS HY
0.1	AQUASOL dATAbASI	23	900	mg	British Natior Suspension
			200	mg	British Natior Tablet
0.00939	Hazardous Substanc	20-25	8	mg	British Natior Tablet
5.84	AQUASOL dATAbASI	25	3500	mg	Buchanan,N., Capsule, Based
0.25	AQUASOL dATAbASI	EFG, pH 6.5 (25)	500	mg	Benet LZ, Bro Tablet
			250	mg	British Natior Tablet
			75	mg	British Natior Tablet
			10	mg	British Natior Tablet (AS DIPI
			30	mg	Fleishaker JC, Tablet (AS mes
			17.5	mg	Diefenbach C Solution (IV 0.2
			0.001	mg	British Natior Capsule
			50	mg	Depierre A, L Tablet
0.525	AQUASOL dATAbASI	25	300	mg	British Natior Tablet
			200	mg	Stavchansky S Capsule (AS BIS
			12.5	mg	British Natior Tablet (AS HYD
			25	mg	http://www.accessdata.fda.g

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185	AQUASOL dATAbASI	pH 10.4 (25)	525	mg	British Natior Solution (IV/IM
			500	mg	Thompson TA Tablet
0.7164	AQUASOL dATAbASI	25	200	mg	British Natior Tablet (AS HYD
0.59	AQUASOL dATAbASI	25	200	mg	Hart J, Hill HM Capsule (AS SO
			150	mg	Nakashima M Tablet
0.0344	Pubchem (AID 1996	pH 7.4 (22.5-24.5), I	150	mg	Benet LZ, Bro Tablet
0.0012	US Patent 2004/6,8:	pH 4-8 (25)	2.5	mg	British Natior Capsule (AS HY
0.5	Cao, D., Wang, J., Zhou, R. et al, J Chem I		1	mg	British Natior Tablets
			200	mg	Sato,R, Tanig Powder (IV/IM
<0.0001	Charman WN, Porter CJ, Mithani S., et a		1000	mg	British Natior Tablet (with Pr
			10	mg/ml	British Natior Solution (IV INJ
			2	mg	Hillas JL, Som Tablet (AS MAL
0.13	AQUASOL dATAbASI	25	100	mg	http://www.a Tablet
			0.457	mg/ml	Benet LZ, Bro Solution (AS HY
			150	mg	Corey AE, Agı Capsule
50	http://www.sigmaa	Sodium salt	5000	mg	Ellis CJ, Gedd Powder (IV INJE
			80	mg	Suh, O.K., Kin Tablet
			20	mg	British Natior Tablet (AS HYD
			50	mg	Keller GA, Cz Tablet (Co-adm
>0.042	Pubchem (AID 1996	pH 7.4 (22.5-24.5)	100	mg	Uchida S, Shi Tablet
			100	mg	Chasseaud LF Tablet
7.43	AQUASOL dATAbASI	37	200	mg	Taguchi M, F Tablet
			16	mg	British Natior Tablet (AS DIHY
>0.0543	Pubchem (AID 1996	pH 7.4 (22.5-24.5)	200	mg	British Natior Tablet (modifie
			50	mg	Shigemitsu T, Tablet (AS HYD
0.257	AQUASOL dATAbASI	25	5	mg	Benet LZ, Bro Tablet
			0.10	%	Martindale, T Ophthalmic (AS
			8	mg	Yang LL, Yuar Capsule (AS HY
			300	mg	Tseng CH, Tai Tablet (AS HYD
>0.0547	Pubchem (AID 1996	pH 7.4 (22.5-24.5)	5	mg	British Natior Tablet
0.1015	AQUASOL dATAbASI	25	5	mg/ml	British Natior Solution (IV AS
0.1	http://www.ema.europa.eu/docs/en_G		2	mg	British Natior Tablet
			20	mg	Tytgat GN., D Tablet
			300	mg	http://www.a Tablet
			200	mg	Northridge D Capsule
26	Cao, D., Wang, J., Zh	20	2800	mg	http://www.a Tablet based or
			1000	mg	FDA Orange E Solution (AS SU
			20	mg	British Natior Tablet
14.85	Harrap KR., Cancer Treat Rev. 1985 Sep;		10	mg/ml	British Natior Solution (IV)
			1000	mg	Wilkinson PJ, Tablet
4	SRC PHYSPROP	25	7.7	mg	British Natior Implant
0.00511	Llinàs A, Glen RC, Gc	Intrinsic (25)	150	mg	FDA Orange E Tablet
			10	mg	Benet LZ, Bro Tablet (AS HYD
			515	mg	Kneer, J., Tan Solution (IV INF
0.16	Koup JR, Dubach UC	pH 5-6	1000	mg	Kneer, J., Tan Tablet
164.41	Auda SH, Mrestani Y	Di sodium salt	3000	mg	Lenfant B, Na Solution (IV INF
			2000	mg	FDA Orange E Solution (IV INF
			2000	mg	Sauermann,R Solution (IV INF
0.4	Khan F, Katara R, Ramteke S., AAPS Phar		200	mg	British Natior Tablet
			4000	mg	FDA Orange E Solution (IV INF
			500	mg	British Natior Tablet
0.0229	AQUASOL dATAbASI	20	400	mg	British Natior Tablet (AS HYD
793	AQUASOL dATAbASI	RT	500	mg	Benet LZ, Bro Capsule
>0.0456	Pubchem (AID 1996	pH 7.4 (22.5-24.5)	10	mg	British Natior Tablet
2	AQUASOL dATAbASI	RT	50	mg	British Natior Capsule
			400	mg	FDA Orange E Tablet (AS HYD

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<10	SRC PHYSPROP		500	mg	Yu JY, Song H Tablet (AS CARI
0.8913	AQUASOL dATAbASI	25	250	mg	FDA Orange E Tablet
			200	mg	Massarella J, Tablet
			0.05	mg	Belch JJ, McL Tablet
>=170	Hazardous Substanc	pH 6-8	75	mg/ml	British Natior Solution (IV INF
			5	mg	British Natior Tablet
		Active metabolite			
			20	mg	Zussman BD, Tablet
0.2724	AQUASOL dATAbASI	25			
0.0367	Pubchem (AID 1996	pH 7.4 (22.5-24.5)	500	mg	FDA Orange E Capsule
			100	mg	British Natior Tablet
			200	mg	British Natior Powder (IV) co
			200	mg	Bron NJ, Dorr Capsule
			30	mg	British Natior Tablet
0.09708	AQUASOL dATAbASI	RT	500	mg	FDA Orange E Capsule
			768	mg	British Natior Capsule (AS OIL
0.0151	Pubchem (AID 1996	pH 7.4 (22.5-24.5)	300	mg	British Natior Tablet (AS SULF
			30000	mg	British Natior Granules (AS H'
<0.001	Crombie AL, Antrilli	TM, Campbell BA., e	20	mg	FDA Orange E Powder (IV INF
			20	mg	Curvall M, Elwin CE, Kazemi-'
0.05	AQUASOL dATAbASI	RT	1	mg	British Natior Tablet
40	AQUASOL dATAbASE	6th edition	50	mg	British Natior Tablet (AS ANH
0.0003176	AQUASOL dATAbASI	22.5	4	mg	British Natior Tablet (AS HYD
			50	mg	British Natior Tablet
			500	mg	British Natior Capsules (AS BI
83.3	SRC PHYSPROP	20	10	mg	FDA Orange E Tablet (Extende
			100	mg	British Natior Capsule (AS SO
			0.50	%	FDA Orange E OPHTHALMIC
			30	mg	Martindale, T Tablet
			2	mg/ml	Eriksson B, O Solutionn (Mou
			0.15	mg	FDA Orange E Tablet (Co adm
			7.5	mg	Demoen PJ., . Tablet
0.1	Llinàs A, Glen RC, Gc	Intrinsic (25)	200	mg	British Natior Tablet
76.9	Hazardous Substances Data Bank (HSDB		20	mg	FDA Orange E Capsule (AS HY
			3	mg	FDA Orange E Tablet (Co adm
			75	mg	FDA Orange E Tablet (AS HYD
0.012	AQUASOL dATAbASI	25	20	mg	British Natior Tablet
0.0141	AQUASOL dATAbASI	25	0.2	mg	Martindale, T Tablet
			40	mg	British Natior Tablets (AS DIH
			1	mg	FDA Orange E Solution (IM, SC
			500	mg	British Natior Tablet (AS FUR(
			100	mg	FDA Orange E Tablet
333	SRC PHYSPROP		800	mg	FDA Orange E Tablet 15mg/kg
			5	mg	British Natior Tablet (AS BRO
0.2	AQUASOL dATAbASI	25	800	mg	British Natior Tablet
			75	mg	British Natior Capsule (AS HY
			16	mg	British Natior Tablets (AS ME
			750	mg	Lencioni M, F Tablet
13.75	AQUASOL dATAbASI	hydrochloride (37)	80	mg	Mahaparale S Tablet (AS HYD
			7000	mg	Martindale, T Powder (IV INF
			75	mg	British Natior Tablet (AS OLA
			50	mg	Antonaccio MJ, Verjee S., Am
0.014	Dage RC, Kariya T, Hsieh CP., et al., Am J		5	mg/ml	British Natior Solution (IV INJ
2.4	Cao, D., Wang, J., Zh	25	1	mg	FDA Orange E Tablet
			5	mg	Benincosa LJ, Tablet
			600	mg	British Natior Tablet (AS MES
			1	mg	FDA Orange E Tablet
			2	mg	British Natior Tablet (sublingu
0.4	Benet LZ, Broccatell	Hydrochloride salt a	150	mg	British Natior Tablet (AS HYD

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~0.001	AQUASOL dATAbASE	30	140	mg	British Natior Capsule (AS PH
			50	mg	FDA Orange E Tablet
1000	SRC PHYSPROP		62	mg/ml	Benet LZ, Bro Solution
0.0014	AQUASOL dATAbASE	25	2	mg	FDA Orange E Tablet
690	SRC PHYSPROP	20	400	mg	FDA Orange E Tablet
0.0189	Pubchem (AID 1996	pH 7.4 (22.5-24.5)	10	mg	Martindale, T Tablet
			200	mg	British Natior Tablet
			400	mg	http://www.a Tablet
0.0129	Khosravan,R., Grabowski, B., Wu, JT., e		120	mg	British Natior Tablet
			900	mg	http://www.a Tablet
0.00842	AQUASOL dATAbASE	25	600	mg	Henson R, Llc Tablet
			20	mg	Caccia S, Con Tablet (AS HYD
0.0008	AQUASOL dATAbASE	25	267	mg	British Natior Capsule (micro
			80	mg	Montes B, Ca Tablet
			150	mg	Fletcher MR, Capsule
0.015	http://www.fda.gov	Neutral pH	200	mg	British Natior Tablet
0.040	AQUASOL dATAbASE	ambient temp	1	mg	British Natior Tablet
			500	mg	British Natior Capsule (AS SO
15	SRC PHYSPROP	25	10	mg/ml	British Natior Solution (IV INF
			0.3	mg	British Natior Tablet (AS ACE
0.0165	Marına,TM., Margarita, VM., Salcedo, G		20	mg	Holmes B, Br Tablet
			78	mg/inhalation	FDA Orange E AEROSOL, MET
			20	mg	FDA Orange E Tablet
1	AQUASOL dATAbASE	6th edition	100	mg	Singal, R., Gu Capsule (AS MA
			1000	mg/ml	FDA Orange E Solution (IV INF
			3000	mg	FDA Orange E Granules (ORAI
			40	mg	British Natior Tablet (AS SOD
			1200	mg	Na-Bangchan Capsule
			2.5	mg	British Natior Tablet (AS SUC
778	AQUASOL dATAbASE	25			
			50	mg	Martindale, T Tablet
			400	mg	Martindale, T Oral
			200	mg	Lin C, Kim H, Capsule
			40	mg/ml	Benet LZ, Bro Solution (IV)
4	SRC PHYSPROP	25			
			50	mg	Martindale, T Tablet
0.0695	Pubchem (AID 1996	pH 7.4 (22.5-24.5)	180	mg	Martindale, T Tablet
			2	mg	Martindale, T Tablet (AS BRO
			500	mg	Gillespie, Dru Tablet
			2	mg	British Natior Tablet (AS HYD
76	Hazardous Substanc	sulfate (25)	25	mg	FDA Orange E Tablet
0.4347	AQUASOL dATAbASE	25	500	mg	Smith, DA., C Tablet
0.3299	AQUASOL dATAbASE	RT	100	mg	FDA Orange E Tablet
1.931	Hazardous Substances Data Bank (HSDB		1.3	mg	British Natior Capsule
			400	mg	FDA Orange E Tablet (AS SULF
			500	mg	FDA Orange E Solution (IM)
1000	SRC PHYSPROP	25	1000	mg	British Natior Capsule
			0.1	mg/ml	FDA Orange E Solution (IV INF
			40	mg	Glue P, White Capsule
			3000	mg	FDA Orange E Powder (IV INF
			20	mg	British Natior Tablet (AS HYD
10	SRC PHYSPROP		1000	mg	FDA Orange E Powder (IV AS (
			100	mg	FDA Orange E Tablet (AS HYD
			200	mg	Tamassia, V., Tablet
6000	Hazardous Substanc	20	60	%	FDA Orange E Solution (IV)
0.5497	AQUASOL dATAbASE	25	30	mg	British Natior Tablet
			40	mg	British Natior Tablet

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			20	mg	British Natior Capsule
			200	mg	Honig WJ, Pe Tablet
			1000	mg	FDA Orange E Capsule (AS SU
			60	mg	Martindale, T Capsule
			0.25	mg	Martindale, T Powder (IV)
			6	mg	British Natior Tablet
~30	http://www.accessc	25	200	mg	British Natior Tablet
0.45	http://www.accessdata.fda.gov/drugsat		25	mg	Martindale, T Tablet
			2.5	mg	British Natior Tablet
			150	mg	Martindale, T Tablet
1040	http://www.ucb.com/_up/ucb_com_pr		750	mg	British Natior Tablet
			0.50	%	FDA Orange E OPHTHALMIC (
0.02	AQUASOL dATAbASI	25	50	mg	British Natior Tablet (AS MAL
			1.5	mg	British Natior Tablet
			50	mg	Dieterle W, F Tablet
			2	mg	Sundberg S, A Tablet/Capsule
0.003958	AQUASOL dATAbASI	37	30	mg	British Natior Tablet (AS SOD
			0.02	mg	Krause W, M Tablet
			0.10	%	FDA Orange E OPHTHALMIC (
<0.05	Hazardous Substances Data Bank (HSDB		250	mg	British Natior Capsule
			1.5	mg	British Natior Tablet
0.0155	Pubchem (AID 1996	pH 7.4 (22.5-24.5)	8	mg	Martindale, T Tablet
			800	mg	Corazziari E, I Tablet
			408	mg	British Natior Capsule
			2.5	mg	Martindale, T Capsule (Co adı
			150	mg	British Natior Tablet (AS HYD
0.03	SRC PHYSPROP		100	mg	Martindale, T Capsule
0.002	Kawabata,Y., Wada, K., Nakatani, M., et		160	mg	British Natior Tablet
6.55	AQUASOL dATAbASI	25	150	mg	British Natior Tablet (AS HYD
			200	mg	British Natior Tablet
0.124	AQUASOL dATAbASI	25	100	mg	British Natior Tablet
			1000	mg	British Natior Powder (IV INJE
			600	mg	British Natior Tablet
0.013	Yin GG, Kookana RS, Ru YJ., Environ Int.		0.15	mg	FDA Orange E Tablet (Co adm
7.2	SRC PHYSPROP	25	1500	mg	British Natior Tablet
2.8	AQUASOL dATAbASI	25	300	mg	FDA Orange E Capsule
			0.2	mg	FDA Orange E Tablet (AS MAL
			750	mg	British Natior Capsule
			20000	mg	FDA Orange E Powder (IV AS S
			40	mg	British Natior Tablet (AS HYD
0.09	AQUASOL dATAbASI	ambient temp	50	mg	British Natior Tablet (Buccal)
0.0004748	AQUASOL dATAbASI	22.5	600	mg	British Natior Tablet
ı saturation occurs Ref: Pharmacokinetics of miglitol : Absorp			100	mg	FDA Orange E Tablet
>1000	http://www.ema.europa.eu/docs/en_G		100	mg	British Natior Capsule
			1	mg/ml	FDA Orange E Solution (IV)
			0.4	mg	British Natior Tablet
0.0001	SRC PHYSPROP	25	3000	mg	British Natior Tablet
			2	mg/ml	British Natior Solution (AS IN.
			200	mg	British Natior Tablet
			15	mg	British Natior Tablet (AS HYD
			4	mg	Martindale, T Tablet
			10	mg	British Natior Tablet (AS SOL
0.02	Alelyunas YW, Liu R,	25	300	mg	FDA Orange E Tablet
			10000	mg	FDA Orange E Powder (IV INF
			400	mg	British Natior Tablet (AS HYD
			80	mg	British Natior Tablet (AS HYD
0.8003	AQUASOL dATAbASE	6th edition	0.6	mg	British Natior Tablet
0.043	Hazardous Substanc	pH 7.4	1500	mg	British Natior Tablet

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0.006	AQUASOL dATAbASI	22.5	1000	mg	British Natior Tablet
			0.8	mg/actuation	FDA Orange E Topical (Nasal)
			200	mg	British Natior Tablet (AS OXA
35	http://www.gsk.con	Hydrochloride	2.5	mg	British Natior Tablet (AS HYD
			180	mg	British Natior Tablet
			2	%	FDA Orange E OPHTHALMIC
0.0326	Pubchem (AID 1996	pH 7.4 (22.5-24.5)	300	mg	FDA Orange E Tablet (AS HYD
			90	mg	British Natior Tablet (AS HYD
			1000	mg	British Natior Tablet (AS SULF
			100	mg/ml	FDA Orange E Solution (IV INF
17.1	AQUASOL dATAbASI	20	1000	mg	FDA Orange E Tablet (extende
			30	mg	British Natior Tablet
			150	mg	FDA Orange E Tablet
			60	mg	Martindale, T Tablet (Prolong
			40	mg	FDA Orange E Tablet (extende
			250	mg	Martindale, The complete dr
21.4	AQUASOL dATAbASI	25	300	mg	British Natior Tablet
			50	mg	Ringoir S, Lan Tablet
			0.25	mg	FDA Orange E Tablet (Co-adm
			120	mg	British Natior Capsule
			1500	mg	FDA Orange E Capsule
			30	mg	Martindale, T Tablet
0.084	Douroumis D, Fahr A. Eur J Pharm Bioph		600	mg	British Natior Tablet
			800	mg	Perucca E, Pa Tablet
			2	mg	Ensing K, de Z Tablet (AS BRO
			96	mg	Wetzelsberge Tablet
0.02	AQUASOL dATAbASI	Intrinsic (RT)	100	mg	FDA Orange E Tablet
7.548	AQUASOL dATAbASI	21	500	mg	British Natior Tablet (AS DIHY
			100	mg	Sigurdsson JA Tablet
500	The Merck Index: 12	25	2	mg/ml	British Natior Solution (BRON
			80	mg	British Natior Tablet (AS SOD
			100	mg	Scatina JA, Hi Tablet/Capsule
7	AQUASOL dATAbASI	RT	80	mg	FDA Orange E Tablet (AS SULF
3	Harnden MR, Jarvest RL, Boyd MR., et al		1	%	British Natior Cream
			100	mg	British Natior Capsule
0.77	AQUASOL dATAbASI	25	200	mg	FDA Orange E Capsule (AS SO
77	SRC PHYSPROP	25	400	mg	FDA Orange E Tablet (extende
			300	mg	Martindale, T Tablet (AS male
			8	mg	British Natior Tablet (AS ERBI
0.182	AQUASOL dATAbASE	6th edition	500	mg	FDA Orange E Tablet
			200	mg	British Natior Tablet
			6	mg	FDA Orange E Tablet
4.2	AQUASOL dATAbASI	25	500	mg	FDA Orange E Capsule
			50	mg	Martindale, T Tablet (AS HYD
0.59	SRC PHYSPROP	37			
5	Chaw CS, Tan CW, Y	pH 7.4			
			0.4	mg	FDA Orange E Per inhalation
			6	mg	Meyer BH, M Tablet
			150	mg	Lee TG, Goldl Capsule
			50	mg	Fauvel JP, Be Tablet
			1.5	mg	Martindale, T Tablet (AS MAL
			4	mg	FDA Orange E Tablet
0.01	http://www.accessdata.fda.gov/drugsat		4	mg	http://www.a Capsule
			1000	mg	British Natior Powder (IV INF
			225	mg	Martindale, T Capsule
0.47	AQUASOL dATAbASI	25	750	mg	British Natior Tablet
0.0036	AQUASOL dATAbASI	22.5	2000	mg	British Natior Tablet

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0.000005	US Patent 2005/0171,203 Serial numbe	500	mg	FDA Orange E Tablet
		500	mg/ml	FDA Orange E Solution (IV INF
		50	mg	British Natior Tablet (AS HYD
		30	mg	British Natior Tablet (AS HYD
		500	mg	Jenner PJ, Ell: Tablet
500	Hazardous Substances Data Bank (HSDB	10	mg	FDA Orange E Tablet (AS HYD
1000	SRC PHYSPROP 25	900	mg	Rasmussen F' Tablet
17.4	AQUASOL dATAbASI EFG (25)	2000	mg	British Natior Tablet
0.01	AQUASOL dATAbASE 6th edition	75	mg	FDA Orange E Tablet
		0.15	mg	British Natior Tablet (AS HYD
		100	mg	FDA Orange E Tablet (AS SOD
		40	mg	British Natior Tablet (AS HYD
		Active metabolite		
0.395	Mallikarjuna Gouda pH 7.5	60	mg	British Natior Tablet (AS SOD
		10	mg	British Natior Tablet
		600	mg	Davies RF, Lir Tablet
		200	mg	Widerlöv E, F Tablet
		20	mg	Lode H, Huet Tablet
		10	mg	Evans, ME., S Tablet
		10	mg	FDA Orange E Tablet (AS HYD
		10	mg	British Natior Tablet (AS BEN
		5	mg	Strandgârder Tablet
0.031	http://www.accessdata.fda.gov/drugsat	1600	mg	British Natior Tablet
4.3	AQUASOL dATAbASI 25	2000	mg	Sweatman TV Tablet
17.95	AQUASOL dATAbASI EFG (25)	8	mg	British Natior Tablet (AS SULF
		750	mg	The AARP Gu Tablet
		5	mg	British Natior Tablet (AS HYD
		100	mg	Shi J, Ripley E Tablet
2.9	Li DX, Jang KY, Kang hydrochloride mon	15	mg	FDA Orange E Capsule
		250	mg	Martindale, T Capsule
		100	mg	British Natior Tablet (AS PHO
		10	mg	British Natior Tablet (AS SUC
		24	mg	FDA Orange E Tablet (AS HYD
		1000	mg	FDA Orange E Powder (IM INJ
5.066	AQUASOL dATAbASI 25	1000	mg	FDA Orange E Powder (IV INJE
0.49	AQUASOL dATAbASI 38			
0.076	AQUASOL dATAbASI 25	0.05	mg/ml	FDA Orange E Powder (IV INF
		5000	mg	FDA Orange E Powder (IV co-a
0.4453	AQUASOL dATAbASI 25	2000	mg	Martindale, T Tablet (Co-adm
2.601	AQUASOL dATAbASI 22	200	mg	British Natior Tablet
1.382	AQUASOL dATAbASI 25			
		400	mg	Martindale, T Tablet
		1	%	FDA Orange E OPHTHALMIC
		1000	mg	Martindale, T Powder (IV INJI
		1	mg	British Natior Tablet (AS HYD
		150	mg	British Natior Tablet (AS HYD
		400	mg	British Natior Powder (IV INJE
0.0929252	Du-Cunya,L., Huwyl Intrinsic, pH 6.5	30	mg	British Natior Tablet
		400	mg	British Natior Capsule
		25	mg	Johansson HE Tablet (AS HYD
		1	mg	Ericsson, H., I Tablet
0.05	AQUASOL dATAbASI Intrinsic (25)	3000	mg	FDA Orange E Tablet
0.001113	AQUASOL dATAbASI 22.5	200	mg	FDA Orange E Tablet
		2.5	mg	British Natior Tablet
		3000	mg	British Natior Powder (IV INF
0.001	Pubchem (AID 1996 pH 7.4 (22.5-24.5)	250	mg	FDA Orange E Tablet (AS HYD
		50	mg	Martindale, Tablet (AS HYD
18.25	Alelyunas YW, Liu R, pH 7.2	8	mg	British Natior Tablet (AS HYD

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			112	mg	British Natior Powder (INHAL
			600	mg	FDA Orange E Tablet (AS HYD
			25	mg/ml	FDA Orange E Solution (IV AS
			400	mg	Lloyd-Jones J Capsule
			200	mg	Passariello N, Tablet
12	http://www.accessc	Tartrate	2	mg	British Natior Tablet (AS TAR
			60	mg	British Natior Tablet (AS CITR
			20	mg	British Natior Tablet
			4	mg	British Natior Capsule
			200	mg	Martindale, T Tablet
0.07999	AQUASOL dATAbASI	25	4	mg	Benet LZ, Bro Tablet
0.041	AQUASOL dATAbASI	25	40	mg/ml	FDA Orange E Solution (IV INJ
0.01223	AQUASOL dATAbASI	24	5	mg	British Natior Tablet (AS HYD
0.0006709	AQUASOL dATAbASI	22.5	5	mg	British Natior Tablet (AS HYD
			10	mg	British Natior Tablet (AS TAR
			150	mg	Greiner,J., Kü Tablet
			5	mg	Martindale, T Capsule
50	Dutcher, JD., . Am. C	Chloride (22)	3	mg/ml	FDA Orange E Solution (IV INJ
			90	mg	Martindale, T Tablet
			500	mg	British Natior Capsule (AS HY
			1	mg	Martindale, T Tablet (AS TAR
16	http://www.aspenp	pH 3, Bromide (25)	10	mg	British Natior Powder (IV INJI
			1000	mg	British Natior Tablet
0.32	http://www.accessc	Hydrochloride	40	mg	FDA Orange E Tablet
0.017	Szuts EZ, Harosi FI., Arch Biochem Bioph		110	mg	Benet LZ, Bro Tablet
0.0209	AQUASOL dATAbASI	33	50	mg/ml	British Natior Solution (ORAL
			30	mg	Taylor, IW., C Capsule
0.058	AQUASOL dATAbASI	25	80	mg	British Natior Tablet
70.98	AQUASOL dATAbASE	6th edition	0.75	mg	FDA Orange E Tablet
18	http://www.accessdata.fda.gov/drugsat		10	mg	FDA Orange E Powder (Inhala
			600	mg	FDA Orange E Tablet
			7.5	mg	http://produ Tablet
			100	mg	Martindale, T Tablet
			6	mg	FDA Orange E Capsule
2.794	AQUASOL dATAbASI	20	50	mg	Popa C, Beck Syrup
0.8	AQUASOL dATAbASI	25	30	mg	British Natior Tablet
0.0095	Robarge KD, Brunto	pH 6.5	150	mg	FDA Orange E Capsule
			800	mg	Shiveley L, St Capsule
32.26	AQUASOL dATAbASE	6th edition	750	mg	Lücker PW, W Capsule
0.006	Boxenbaum HG, Pos	pH 7.4 (37)	2	mg	Martindale, T Tablet
			100	mg	British Natior Tablet
			300	mg	FDA Orange E Capsule (AS HY
13.6	http://www.ema.europa.eu/docs/en_G		100	mg	FDA Orange E Tablet (Extende
0.2118	AQUASOL dATAbASI	25	50	mg/ml	FDA Orange E Powder (IV co-a
0.12	AQUASOL dATAbASI	25	100	mg	FDA Orange E Tablet
			20	mg	Krause W, Sc Tablet
0.013	AQUASOL dATAbASI	25	720	mg	British Natior Tablet (AS MYC
			500	mg	Atkinson AJ J Tablet (AS HYD
			45	mg	FDA Orange E Tablet (AS HYD
0.01	http://www.accessc	25	20	mg	FDA Orange E Tablet
			200	mg	Van Durme, J Capsule
30	AQUASOL dATAbASI	Intrinsic	400	mg	FDA Orange E Tablet (AS MES
			20	mg	Caccia S, Con Tablet
<0.0003	Pubchem (AID 1996	pH 7.4 (22.5-24.5)	30	mg	British Natior Tablet
			450	mg	British Natior Capsule (AS HY
			2	%	FDA Orange E Shampoo
			40	mg	Laufen H, Lei Tablet

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			Active metabolite		
			50	mg	British Natior Tablet (AS CITR
			300	mg	Holmes C, Wl Capsule
			1000	mg	FDA Orange E Powder (IV INF
			35	mg	British Natior Capsule
0.295	SRC PHYSPROP	37	20	mg	Tüber U, Pos Tablet
			2.5	mg	British Natior Tablet
			0.8	mg	British Natior Tablet (AS HYD
			60	mg	FDA Orange E Tablet (AS DIPC
			400	mg	Cottrell PR, Streete JM, Berry
112	Benet LZ, Broccatelli F, Oprea TI., AAPS J		200	mg	British Natior Capsule
			2	mg	FDA Orange E Tablet
			2	mg	FDA Orange E Tablet
			10	mg	FDA Orange E Tablet (AS HYD
0.3215	AQUASOL dATAbASI	0.05N NaCl (25)	400	mg	Martindale, T Tablet
			600	mg	Täuber U, Be Tablet
			500	mg	FDA Orange E Tablet
			10	mg	El-Brashy, A., Tablet
0.002343	AQUASOL dATAbASE	6th edition			
			40	mg	British Natior Tablet (AS DIHY
			10	mg	FDA Orange E Tablet
			0.5	mg	British Natior Capsule (AS HY
			250	mg	British Natior Capsule
			300	mg	Berry H, Coq Tablet
2.5	SRC PHYSPROP	25	200	mg	FDA Orange E Tablet
			50	mg	Fillastre, JP., / Tablet (AS HYD
			500	mg	British Natior Solution (IV INF
0.02	AQUASOL dATAbASI	21			
			0.5	mg	British Natior Capsule
0.0106	AQUASOL dATAbASI	pH 3 (25)	250	mg	Marks JW, Bc Tablet (Unequa
			600	mg	FDA Orange E Tablet (extende
0.003533	AQUASOL dATAbASI	pH 3 (25)	850	mg	British Natior Tablet
			10	mg	Martindale, T Tablet
			3000	mg	British Natior Dispersable Tal
~0.04	www.novartis.com.a	37	2000	mg	Martindale, T Tablet made in
0.01	http://www1.astraz	RT	180	mg	http://www.a Tablet
			50	mg	British Natior Tablet
0.091	AQUASOL dATAbASE	6th edition	50	mg	Martindale, T Capsule
			1000	mg	FDA Orange E Solution (IV INJ
77.8	AQUASOL dATAbASI	10	500	mg	Moertel CG, / Tablet
			5000	mg	Lim JK., Kisae Powder (Oral)
			25	mg	British Natior Tablet (AS CHL(
0.0420	AQUASOL dATAbASI	22.5	2.5	mg	FDA Orange E Tablet (AS GLU(
500	Hazardous Substanc	25	66	%	FDA Orange E Solution (Oral)
1	SRC PHYSPROP		500	mg	FDA Orange E Tablet
			755	mg	Benet LZ, Bro Solution (ORAL
			10000	mg	Martindale, T Powder (IV INF
			10.5	%	Martindale, T Powder (IV INF
			0.042	mg	FDA Orange E Inhalation (AS E
			250	mg	Bentur Y, Rail Powder (IV INF
			15	mg/ml	British Natior Solution (SODI(
			10	mg/ml	FDA Orange E Solution (IV)
			30	mg	British Natior Tablet (AS BRO
			0.2	mg/ml	British Natior Solution (IV AS

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Transport route	*Transport Reference*	*Transporter symbol*	*Transporter comments*	*MP (°C)*	*MP Reference*
IUM)					
DROCHLORIDE)				157	Hazardous Substances Data Bank (HSDB)
Paracellular	Saitoh R, Su	*		221.5	MSDS Sigma aldrich http://www.sigmaalc
sium salt				120	Chemfinder DEMO PerkinElmer Imformat
Carrier med	Varma MV,	E			
Carrier med	Estudante M	E		204	Hazardous Substances Data Bank (HSDB)
Carrier Med	Wang Q, Ra	E			
Carrier med	Estudante M	I		194	Hazardous Substances Data Bank (HSDB),
Carrier med	Varma MV,	E			
Carrier med	Estudante M	I		255	SRC PHYSPROP
Paracellular,	Pharmacoki	I*		206.75	SRC PHYSPROP
Carrier med	Estudante M	B			
Carrier med	Stenberg P,	B		178	SRC PHYSPROP
/DRATE)					
Carrier Med	Ogihara T, K	B		194	http://www.roche.com/pages/csds/engli
Carrier med	Stewart BH,	I		164	Hazardous Substances Data Bank (HSDB)
Carrier med	Estudante M	E			
	Seral, C.,Mic	E		187.5	Hazardous Substances Data Bank (HSDB)
Carrier med	Sai, Y., Tsuji.	I		250	SRC PHYSPROP
Carrier med	Estudante M	E		220	SRC PHYSPROP
				116.50	Hazardous Substances Data Bank (HSDB)
Carrier med	Varma MV,	E*		142	SRC PHYSPROP
CINATE)				170	Hazardous Substances Data Bank (HSDB)
Carrier med	Varma MV,	E			
Carrier med	Collett A, Sir	A		69.5	SRC PHYSPROP
NOHYDRATE HEMI-ETHANOLATE)				114	SRC PHYSPROP
Carrier med	Lee K, Ng C,	E*		163.5	SRC PHYSPROP
Carrier med	Gao S, Singh	I		155.5	SRC PHYSPROP
AS HYDROCHLORIDE)				172.5	SRC PHYSPROP
				350	SRC PHYSPROP
Paracellular	Lacombe O,	*			
Carrier Med	Li J, Volpe D.	B			
Carrier med	Varma MV,	B		191	SRC PHYSPROP
Carrier med	Thwaites DT	I		207	SRC PHYSPROP
Paracellular	Hilgendorf C	*		295	SRC PHYSPROP
Carrier med	Estudante M	B			
Carrier med	Hu, M.; Che	I			
Paracellular	Collett A, Sir	*		274	SRC PHYSPROP
Paracellular	Karlsson J, U	*		168	SRC PHYSPROP
Carrier med	Estudante M	E		213.5	Hazardous Substances Data Bank (HSDB)
Paracellular	Hilgendorf C	*			
Carrier med	Schmitt U, A	E		126.5	SRC PHYSPROP
Paracellular	Hilgendorf C	I*		147	SRC PHYSPROP
Carrier med	Estudante M	I		300	SRC PHYSPROP
				114.5	SRC PHYSPROP
				135	SRC PHYSPROP
Carrier med	Estudante M	E		194.5	Hazardous Substances Data Bank (HSDB),
Carrier Med	Estudante M	B		256	Hazardous Substances Data Bank (HSDB)
Carrier med	Estudante M	E		230	SRC PHYSPROP

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Carrier med Knox C, Law	E		130	SRC PHYSPROP
Carrier med Pauli-Magnu	B		249	SRC PHYSPROP
Carrier med Troutman M	B		121	SRC PHYSPROP
Carrier med Soldner A, B	E		184	SRC PHYSPROP
CLATE)			201	AQUASOL dATAbASE 6th edition
Carrier med Varma MV,	E		242.5	SRC PHYSPROP
ROCHLORIDE)			244	SRC PHYSPROP
Carrier med Susanto M,	B	Medium to low affinity for PEPT1		
Carrier med Varma MV,	E		243.5	SRC PHYSPROP
Carrier med Varma MV,	E		222	SRC PHYSPROP
			94.75	SRC PHYSPROP
Carrier med Varma MV,	E			
Carrier Med Estudante M	I	Poor subsrate	143.75	Hazardous Substances Data Bank (HSDB)
Carrier med Crivori , P., F	E		226	Hazardous Substances Data Bank (HSDB)
Carrier med Varma MV,	E		112.5	SRC PHYSPROP
			248	SRC PHYSPROP
Carrier med Estudante M	E		163	SRC PHYSPROP
/kg at 70 kg adult)			150.5	SRC PHYSPROP
TATE)			146	SRC PHYSPROP
Carrier med Faassen F, V	E		196.5	SRC PHYSPROP
NOHYDRATE)				
Carrier med Estudante M	E			
ROCHLORIDE)			293.5	Chemfinder DEMO PerkinElmer Imformat
Carrier med Buyse,M., B	I			
Efflux, pgp http://www	E			
Carrier med Varma MV,	E		146	SRC PHYSPROP
			254	SRC PHYSPROP
Carrier med Varma MV,	E		289	SRC PHYSPROP
Carrier med Varma MV,	E		122	Morissette SL, Soukasene S, Levinson D.,
DROCHLORIDE)			180.5	Hazardous Substances Data Bank (HSDB)
Carrier med Crivori , P., F	E		235	SRC PHYSPROP
TATE)			203.5	SRC PHYSPROP
Carrier med Estudante M	B		114	SRC PHYSPROP
Carrier med Estudante M	E			
ECTION AS SULFATE)			118.5	SRC PHYSPROP
Carrier med Kim WY, Ber	E		183	SRC PHYSPROP
Carrier med Knox C, Law	E		183.5	SRC PHYSPROP
Carrier Med MacDonald	I		191	SRC PHYSPROP
Carrier med Varma MV,	E		201	SRC PHYSPROP
			>300	Hazardous Substances Data Bank (HSDB),
Carrier med Varma MV,	E		147	SRC PHYSPROP
			174.5	Hazardous Substances Data Bank (HSDB),
Carrier med Estudante M	E		279	SRC PHYSPROP
Carrier med Knox C, Law	E	Substrate/inhil	151.5	SRC PHYSPROP
Carrier med Varma MV,	B		174	SRC PHYSPROP
Carrier med Dilger K, Sch	E		234	SRC PHYSPROP
DIUM SALT)				
ROBROMIDE)			182.5	Hazardous Substances Data Bank (HSDB),
Carrier med Knox C, Law	E		232.5	SRC PHYSPROP
ROCHLORIDE)				
ROCHLORIDE)			193	Hazardous Substances Data Bank (HSDB)
ole)			59	SRC PHYSPROP
ed release)			273	SRC PHYSPROP
			147.25	SRC PHYSPROP

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Carrier med Knox C, Law	E	Conflicting res	174.5	SRC PHYSPROP
Carrier Med Varma MV,	E		149.1	SRC PHYSPROP
Carrier med Mashayekhi	E		255	SRC PHYSPROP
ROCHLORIDE)			188	SRC PHYSPROP
Carrier med Vautier S, La	E			
ROCHLORIDE)			87	SRC PHYSPROP
Carrier med Varma MV,	E		262	SRC PHYSPROP
inistered with PHENAZOPYRIDINE HYDROCHLORIDE; SU			139	SRC PHYSPROP
			34	SRC PHYSPROP
Carrier med Knox C, Law	E		170	SRC PHYSPROP
TRATE)			196	SRC PHYSPROP
IUM OR POTASSIUM)			157	SRC PHYSPROP
Carrier med Knox C, Law	E		180	Hazardous Substances Data Bank (HSDB)
TRATE)				
			167	SRC PHYSPROP
Carrier med Varma MV,	E		288.5	SRC PHYSPROP
ROCHLORIDE)			99.5	Hazardous Substances Data Bank (HSDB)
Carrier med Choi JS, Jin M	I		94	SRC PHYSPROP
Carrier med Choi MK, So	E		188	Hazardous Substances Data Bank (HSDB)
Carrier med Varma MV,	E		135	SRC PHYSPROP
Carrier Med Estudante M	B		169	SRC PHYSPROP
			110.5	SRC PHYSPROP
			247	http://www.roche-australia.com/fmfiles/
			153	SRC PHYSPROP
Carrier med Varma MV,	E		<25	SRC PHYSPROP
DROCHLORIDE)			219	SRC PHYSPROP
DIUM)			286	SRC PHYSPROP
Carrier med Estudante M	E			
			< 25	SRC PHYSPROP
ROCHLORIDE)				
Carrier med Estudante M	E		220	SRC PHYSPROP
			238	SRC PHYSPROP
			215.5	SRC PHYSPROP
Carrier med Knox C, Law	I		128.5	SRC PHYSPROP
ROCHLORIDE)				
			234	Hazardous Substances Data Bank (HSDB)
Carrier med Faassen F, V	E	Subsrate and i	170	SRC PHYSPROP
Carrier med Knox C, Law	E		76	SRC PHYSPROP
			132	SRC PHYSPROP
			161	Hazardous Substances Data Bank (HSDB)
Carrier med Varma MV,	E		212	Hazardous Substances Data Bank (HSDB)
			228.25	Hazardous Substances Data Bank (HSDB)
HYDROCHLORIDE INJECTION)			140.8	SRC PHYSPROP
ROCHLORIDE)			169	SRC PHYSPROP
			180	SRC PHYSPROP
ROCHLORIDE)			60	SRC PHYSPROP
EATE)			<25	AQUASOL dATAbASE 6th edition
			183.5	SRC PHYSPROP
Carrier med Knox C, Law	E		96	SRC PHYSPROP
IUM)			161	SRC PHYSPROP
			108	SRC PHYSPROP
			158	SRC PHYSPROP
			190.2	SRC PHYSPROP
			178	Hazardous Substances Data Bank (HSDB)
Carrier med Estudante M	B		<25	SRC PHYSPROP
Carrier med Varma MV,	E		159	SRC PHYSPROP
ROCHLORIDE)			130	SRC PHYSPROP
Carrier med Knox C, Law	E		202	SRC PHYSPROP

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Carrier Med Shugarts, S.	I		216	MSDS Sigma aldrich http://www.sigmaalc
			114	SRC PHYSPROP
			171	SRC PHYSPROP
			228	SRC PHYSPROP
Carrier med Varma MV,	E			
Carrier med Varma MV,	E		137	SRC PHYSPROP
ECTION)			68.5	SRC PHYSPROP
			199	SRC PHYSPROP
Carrier med Knox C, Law	E		97	SRC PHYSPROP
Carrier med Varma MV,	E		173	SRC PHYSPROP
Carrier med Luna-Tortós	E		177	Chemfinder DEMO PerkinElmer Imformat
ROCHLORIDE)				
IDECANOATE OILY SOLUTION)			155	SRC PHYSPROP
			233.5	Hazardous Substances Data Bank (HSDB),
Carrier med Wolf DC, Ho	E		181	SRC PHYSPROP
nized)			121	SRC PHYSPROP
Carrier med Lennernäs H	I		285	SRC PHYSPROP
IUM FORM)			234	SRC PHYSPROP
USION) AS MESILATE			140	SRC PHYSPROP
DIUM SALT)			250	SRC PHYSPROP
Carrier med Therapeutic	I		245	Hazardous Substances Data Bank (HSDB)
ECTION/INFUSION)			184	http://www.pfizer.ca/en/our_products/p
Carrier med Estudante M	I*			
Paracellular Matsson P, I	*		80	SRC PHYSPROP
ROCHLORIDE)				
SODIUM INFUSION)				
Carrier med Estudante M	I		200	SRC PHYSPROP
ECTION/ORAL SUSPENSION)			170	Hazardous Substances Data Bank (HSDB)
ROCHLORIDE)			148.5	SRC PHYSPROP
			241	SRC PHYSPROP
Carrier med Estudante M	E			
ATE)			100	SRC PHYSPROP
Carrier med Callegari E, I	E			
			257.25	Hazardous Substances Data Bank (HSDB),
Carrier Med Shugarts, S.	I		167	Hazardous Substances Data Bank (HSDB)
ROCHLORIDE WITH ATROPINE SULFATE)			221.25	Hazardous Substances Data Bank (HSDB)
- extended release			260.5	SRC PHYSPROP
les)			161.5	SRC PHYSPROP
Paracellular Matsson P, I	*		169	SRC PHYSPROP
			283	SRC PHYSPROP
Carrier Med Ogihara T, K	B			
			216	SRC PHYSPROP
ECTION)				
ECTION)			150.5	SRC PHYSPROP
Carrier med Estudante M	I			
Paracellular Pharmacoki	*	No experimental results but 2 sources states this route		
Carrier Med Bretschneid	B		208	SRC PHYSPROP
Carrier med Estudante M	E			
Carrier med Menon RM,	I			
Carrier med Varma MV,	E		149.5	SRC PHYSPROP
			>300	SRC PHYSPROP
MIDE)				
ISETIONATE)				
Carrier med Santini D, Vi	I		289.5	Hazardous Substances Data Bank (HSDB)

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Carrier med Walker DK, /	E		197.5	Hazardous Substances Data Bank (HSDB)
:IUM)				
			296.5	van Beek TA., Bioorg Med Chem. 2005 Se
Paracellular Matsson P, I	*		300	SRC PHYSPROP
			187	Hazardous Substances Data Bank (HSDB)
Carrier med Kis O, Zastre	B	Possible inhibitory effects		
Carrier med Wenzel U, K	I			
Carrier med Estudante M	I*		219	Hazardous Substances Data Bank (HSDB)
ıinistered NADOLOL)			222	SRC PHYSPROP
netabolite)			149.5	SRC PHYSPROP
			208	SRC PHYSPROP
Carrier med Luckner P, B	I	Moderate affinity for PEPT1		
:CTION/INFUSION AS SODIUM SALT)				
:CTION AS SODIUM SALT)				
Carrier med Estudante M	B			
Carrier med Morrissey K	E		250	SRC PHYSPROP
ACETATE)				
.EATE OR MESILATE)				
ROCHLORIDE)				
Carrier med Choi MK, So	E			
			148	SRC PHYSPROP
Carrier med Behrens I, K	I		140	SRC PHYSPROP
·econ as sodium salt				
ECTION)				
ROCHLORIDE)			145	Hazardous Substances Data Bank (HSDB)
Carrier med Knox C, Law	I			
alation			139	Hazardous Substances Data Bank (HSDB)
Carrier med Merino G, A	E		227.5	SRC PHYSPROP
Carrier med Crivori , P., F	E			
drate of the sodium salt)			178.5	SRC PHYSPROP
			135	SRC PHYSPROP
			235.5	SRC PHYSPROP
ECTION)			199	Hazardous Substances Data Bank (HSDB),
Carrier med Garver E, Hu	E		220	SRC PHYSPROP
			239.75	SRC PHYSPROP
			128.5	http://www.accessdata.fda.gov/drugsatf
			185.5	Hazardous Substances Data Bank (HSDB)
			206	SRC PHYSPROP
			160.5	SRC PHYSPROP
Carrier med Whomsley F	E	Weak subsrate		
:USION/INJECTION)			160.25	SRC PHYSPROP
			159.5	AQUASOL dATAbASE 6th edition
ROCHLORIDE)				
			256	SRC PHYSPROP
ROCHLORIDE)			183	http://www.amgen.ca/Sensipar.pdf
			222	SRC PHYSPROP
			183	SRC PHYSPROP
Carrier med Ozawa N, Sh	E			
			209	SRC PHYSPROP
Carrier med Harrison A, I	E			
			182	Hazardous Substances Data Bank (HSDB)
Carrier med Tolle-Sande	E			
			255.5	SRC PHYSPROP

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Carrier med Gnoth MJ, B	E			
ROCHLORIDE)			273	SRC PHYSPROP
			280	SRC PHYSPROP
			156	SRC PHYSPROP
Carrier med Sai, Y., Tsuji.	I			
ROCHLORIDE)			179	Bernstein CD, Albrecht KL, Marcus DA., Ex
			226	SRC PHYSPROP
AS HYDROCHLORIDE)				
			105	SRC PHYSPROP
ROCHLORIDE)			< 25	SRC PHYSPROP
			175.5	SRC PHYSPROP
CIUM SALT)			< 25	SRC PHYSPROP
Carrier med Jin HE, Song	E		236	Hazardous Substances Data Bank (HSDB)
			191	SRC PHYSPROP
Carrier med Estudante M	I		134.5	SRC PHYSPROP
Carrier med Taubert D, v	E			
ILATE)			278	Hazardous Substances Data Bank (HSDB),
/DROCHLORIDE)			238	http://www.lundbeck.com/upload/ca/en
ATE)			48	SRC PHYSPROP
			167	SRC PHYSPROP
Carrier med Estudante M	I		158	SRC PHYSPROP
			158	SRC PHYSPROP
ROCHLORIDE)			172.5	SRC PHYSPROP
Carrier med Knox C, Law	E			
FATE)				
			106	SRC PHYSPROP
			270	SRC PHYSPROP
			164	MSDS Sigma aldrich http://www.sigmaald
			100	SRC PHYSPROP
Carrier med Goto Y, Itaga	I	No exact detai	262	Hazardous Substances Data Bank (HSDB),
JECTION)			18	SRC PHYSPROP
ger presecribed as oral now only IV			295	SRC PHYSPROP
			254	SRC PHYSPROP
			230.5	SRC PHYSPROP
EATE)			< 25	SRC PHYSPROP
Carrier Med Skerjanec, A	E			
Carrier Med Fine KD, San	I		83	SRC PHYSPROP
Carrier med http://www	E	Weak subsrate	198.5	www.novartis.ca/asknovartispharma
Carrier med Toyobuku H	B		160	SRC PHYSPROP
Carrier med Estudante M	I		283	SRC PHYSPROP
inistered with ethinylestradiol)			197.9	SRC PHYSPROP
			192	SRC PHYSPROP
			192	Hazardous Substances Data Bank (HSDB)
			146.5	SRC PHYSPROP
			209	Ramana, MV., Himaja, M., Dua, K., et al.,
TRIDGE			-79	SRC PHYSPROP
Carrier med Crivori , P., F	E		211	SRC PHYSPROP
			181	SRC PHYSPROP
			271	SRC PHYSPROP
DROCHLORIDE)			180.5	Hazardous Substances Data Bank (HSDB)
Carrier med Estudante M	E			

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Carrier med Kuwayama I	I		315	SRC PHYSPROP
			125.5	Hazardous Substances Data Bank (HSDB)
			127.5	SRC PHYSPROP
			248	Hazardous Substances Data Bank (HSDB)
			207	Chemfinder DEMO PerkinElmer Imformat
FATE)			57	SRC PHYSPROP
ROCHLORIDE)			119	SRC PHYSPROP
			173.5	SRC PHYSPROP
DROCHLORIDE)			147.5	SRC PHYSPROP
			134.5	SRC PHYSPROP
			231	SRC PHYSPROP
			46.5	SRC PHYSPROP
			163	SRC PHYSPROP
			171	Hazardous Substances Data Bank (HSDB)
FATE)			>300	Hazardous Substances Data Bank (HSDB)
			183	SRC PHYSPROP
			176	SRC PHYSPROP
Carrier med Sai, Y., Tsuji.	I		258	SRC PHYSPROP
ROCHLORIDE)			71	SRC PHYSPROP
			136	SRC PHYSPROP
			146	SRC PHYSPROP
Carrier med Estudante M	I		125	SRC PHYSPROP
DIUM)				
			134.5	MSDS Sigma aldrich http://www.sigmaalc
Carrier Med Therapeutic	I		262	SRC PHYSPROP
			191.5	SRC PHYSPROP
			156	SRC PHYSPROP
			71	SRC PHYSPROP
SPHATE)			154	Chemfinder DEMO PerkinElmer Imformat
ROCHLORIDE)			114	SRC PHYSPROP
			219	SRC PHYSPROP
			216.5	SRC PHYSPROP
ROGEN FUMARATE)			151	Chemfinder DEMO PerkinElmer Imformat
			205.5	SRC PHYSPROP
DROCHLORIDE)			204	SRC PHYSPROP
Carrier med Sai, Y., Tsuji.	I	absorption bot	210	Chemfinder DEMO PerkinElmer Imformat
ROCHLORIDE)			88	SRC PHYSPROP
Carrier med Cummins CL	E		184	Hazardous Substances Data Bank (HSDB)
ROCHLORIDE)			126.5	Hazardous Substances Data Bank (HSDB)
MIDE)			153	Hazardous Substances Data Bank (HSDB)
Carrier med Estudante M	B		226	Hazardous Substances Data Bank (HSDB)
Carrier med Shaik N, Giri	E			
Carrier med Varma MV,	E			
Carrier med Estudante M	E		263	SRC PHYSPROP
Carrier med http://www	E		259.5	Hazardous Substances Data Bank (HSDB)
ILATE)				
ILATE)			170.5	Hazardous Substances Data Bank (HSDB)
			226	SRC PHYSPROP
Carrier med Varma MV,	E			
ed beads)				

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ROBROMIDE)				
DROCHLORIDE)				
Carrier med Varma MV,	E		195	SRC PHYSPROP
			160.5	SRC PHYSPROP
Carrier med Moons T, de	E	Intermediate affinity		
ROCHLORIDE)			192	Hazardous Substances Data Bank (HSDB)
ROCHLORIDE)			103	Hazardous Substances Data Bank (HSDB)
			171.4	SRC PHYSPROP
Carrier med Knox C, Law	E		172.5	Hazardous Substances Data Bank (HSDB)
SYLATE)			75.5	SRC PHYSPROP
IUM)				
			64.5	SRC PHYSPROP
ROCHLORIDE)				
ROGEN TATRATE)				
ROCHLORIDE)			74.5	Hazardous Substances Data Bank (HSDB)
			161.5	Hazardous Substances Data Bank (HSDB)
ıRTRATE co-administered with ACETAMINOPHEN)			198	SRC PHYSPROP
Carrier med Knox C, Law	E			
			97	SRC PHYSPROP
			237.5	SRC PHYSPROP
.EATE)				
			114	Hazardous Substances Data Bank (HSDB)
ROCHLORIDE)			214	Hazardous Substances Data Bank (HSDB)
			154	Hazardous Substances Data Bank (HSDB)
ROCHLORIDE)			129.5	Hazardous Substances Data Bank (HSDB)
			138	Chemfinder DEMO PerkinElmer Imformat
DROCHLORIDE)			189.5	SRC PHYSPROP
			225	SRC PHYSPROP
			62	SRC PHYSPROP
ALEATE)			45	SRC PHYSPROP
			263	SRC PHYSPROP
ECTION AS HYDROCHLORIDE)			218	Hazardous Substances Data Bank (HSDB)
ROCHLORIDE)			93	SRC PHYSPROP
Carrier med Knox C, Law	E		174	SRC PHYSPROP
DROCHLORIDE)			< 25	SRC PHYSPROP
ECTION)			202	SRC PHYSPROP
			144.5	MSDS Sigma aldrich http://www.sigmaald
ROCHLORIDE)			86	SRC PHYSPROP
ROCHLORIDE)			141.5	Hazardous Substances Data Bank (HSDB)
DROCHLORIDE)			79.5	SRC PHYSPROP
			229.5	SRC PHYSPROP
			197	SRC PHYSPROP
on 50/mg/kg being dosed and the average man being 7			114.3	SRC PHYSPROP
			189	AQUASOL dATAbASE 6th edition
			178.5	SRC PHYSPROP
			229	SRC PHYSPROP
VOXIL FORM)			>250	Hazardous Substances Data Bank (HSDB)
ylate), never made to market				
.5 mg/kg INFUSION) based on average human being 70kg				
			136	SRC PHYSPROP
			139	SRC PHYSPROP
Carrier med Pang KS., Dr	I		350	SRC PHYSPROP
ıMESYLATE)				
ROGEN MALATE)				
gov/drugsatfda_docs/label/2013/022271s000lbl.pdf				

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I AS SULFATE INJECTION/INFUSION) based on average h			203.5	SRC PHYSPROP
			149.5	SRC PHYSPROP
ROCHLORIDE)			156	Hazardous Substances Data Bank (HSDB)
DIUM)			157	SRC PHYSPROP
			175.5	SRC PHYSPROP
DROCHLORIDE)			>280	Hazardous Substances Data Bank (HSDB)
			81.5	Hazardous Substances Data Bank (HSDB)
INJECTION)				
oguanil hydrochloride) if taken as oral suspension 150m			217.5	MSDS Sigma aldrich http://www.sigmaalc
ECTION AS BESILATE)				
.EATE)				
			243.5	SRC PHYSPROP
'DROCHLORIDE Ophthalmic)			227	Hazardous Substances Data Bank (HSDB)
ECTION)				
			219.5	SRC PHYSPROP
ROCHLORIDE)				
ıinistered Levodopa)				
			151	SRC PHYSPROP
'DROCHLORIDE)			152	Chemfinder DEMO PerkinElmer Imformat
			< 25	SRC PHYSPROP
d release value increases to 400mg)			186	SRC PHYSPROP
ROCHLORIDE)				
Carrier Med Therapeutic	I		232	SRC PHYSPROP
S SODIUM)				
DROCHLORIDE)			238	SRC PHYSPROP
ROCHLORIDE)				
			230.5	SRC PHYSPROP
ANHYDROUS HYDROCHLORIDE)			107.5	SRC PHYSPROP
			287	SRC PHYSPROP
			143	Hazardous Substances Data Bank (HSDB),
Carrier med http://www	E	Weak pgp subsrate		
n surface area			115.5	Hazardous Substances Data Bank (HSDB)
ILFATE)			250.5	Hazardous Substances Data Bank (HSDB)
			123.5	SRC PHYSPROP
			31	SRC PHYSPROP
			197.5	SRC PHYSPROP
ROCHLORIDE)				
FUSION)				
FUSION)				
FUSION/INJECTION)				
FUSION)				
Carrier med Shugarts, S.	I			
			134.2	Arora SC, Sharma PK, Irchhaiya R., et al., J
Carrier med Kato Y, Miya	B		111	SRC PHYSPROP
			57	SRC PHYSPROP
			65	SRC PHYSPROP
			236.2	SRC PHYSPROP
ROCHLORIDE WITH ATOVAQUONE)			129	SRC PHYSPROP

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BAMATE)			78	SRC PHYSPROP
			128	SRC PHYSPROP
			103.5	SRC PHYSPROP
FUSION)			260	MSDS Sigma aldrich http://www.sigmaalc
Carrier med Knütter I, W	I	Medium affinity for transporter		
			265	SRC PHYSPROP
			261	SRC PHYSPROP
			115	SRC PHYSPROP
administered with with ticarcillin				
			253	MSDS Sigma aldrich http://www.sigmaalc
			< 25	SRC PHYSPROP
LY BASE)				
FATE)			184	Hazardous Substances Data Bank (HSDB),
YDROCHLORIDE)				
USION AS HYDROCHLORIDE)				
Vala E, et al., Eur J Clin Pharmacol. 1990;38(3):281-7.			41	SRC PHYSPROP
			238	SRC PHYSPROP
YDROUS)			51.5	SRC PHYSPROP
ROCHLORIDE)			112.8	SRC PHYSPROP
			200.5	Hazardous Substances Data Bank (HSDB)
TARTRATE)			98	SRC PHYSPROP
ed release)			158.5	SRC PHYSPROP
DIUM)			279.5	SRC PHYSPROP
uthwash)				
inistered with ethinyl estradiol)			109.5	SRC PHYSPROP
			182	SRC PHYSPROP
			330.5	SRC PHYSPROP
DROCHLORIDE)			165	Hazardous Substances Data Bank (HSDB),
inistered with estradiol valerate)			214	http://www.bayerresources.com.au/reso
ROCHLORIDE)				
			170.5	SRC PHYSPROP
Carrier med Morrissey KI	E		255.5	SRC PHYSPROP
YDROCODEINE TARTRATE)			112.5	SRC PHYSPROP
C AS MESYLATE)				
OATE)				
g based on body weight			161.5	SRC PHYSPROP
MIDE)				
			71.5	SRC PHYSPROP
DROCHLORIDE)			56	SRC PHYSPROP
SILATE)				
			190	SRC PHYSPROP
ROCHLORIDE Co-adminsitered with paracetemol)				
USION)				
Carrier med Allred AJ, Bc	E			
n J Cardiol. 1986 Aug 29;58(5):114C-116C.				
ECTION)			256	SRC PHYSPROP
ILATE)			249	Hazardous Substances Data Bank (HSDB)
			192	MSDS http://www.sciencelab.com/msds.
ual AS TARTRATE)			213.5	SRC PHYSPROP
Carrier med de Vries NA,	E		229	Hazardous Substances Data Bank (HSDB)

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OSPHATE)		104.5	SRC PHYSPROP
		122.5	SRC PHYSPROP
		-114.1	SRC PHYSPROP
		126	SRC PHYSPROP
		> 300	MSDS Sigma aldrich http://www.sigmaalc
		147.5	SRC PHYSPROP
		206.5	http://www.accessdata.fda.gov/drugsatf
		151.5	SRC PHYSPROP
		112	SRC PHYSPROP
ROCHLORIDE)		167.5	Hazardous Substances Data Bank (HSDB),
nised)		80.5	SRC PHYSPROP
		156.5	SRC PHYSPROP
Carrier med http://www	E		
		253	SRC PHYSPROP
DIUM SALT)			
FUSION)		296	SRC PHYSPROP
TATE)		233.5	Hazardous Substances Data Bank (HSDB)
ERED; INHALATION			
		270	SRC PHYSPROP
ALEATE)		115.5	SRC PHYSPROP
FUSION)			
L SUSPENSION)		94	SRC PHYSPROP
Carrier med Estudante M	E		
CINATE)			
Carrier med Therapeutic	I	119	Chemfinder DEMO PerkinElmer Imformat
		192.5	SRC PHYSPROP
		136	MSDS Sigma aldrich http://www.sigmaalc
		162	MSDS Sigma aldrich http://www.sigmaalc
		105	SRC PHYSPROP
		215	SRC PHYSPROP
		333.5	van Beek TA., Bioorg Med Chem. 2005 Se
		181	SRC PHYSPROP
MIDE)		192.5	SRC PHYSPROP
		153	SRC PHYSPROP
ROCHLORIDE)			
		214.25	Hazardous Substances Data Bank (HSDB),
		146.5	SRC PHYSPROP
		270.5	SRC PHYSPROP
		266.5	Hazardous Substances Data Bank (HSDB)
FATE)		90	SRC PHYSPROP
		119	Chemfinder DEMO PerkinElmer Imformat
		141	SRC PHYSPROP
FUSION AS FUMARATE)		118	Hazardous Substances Data Bank (HSDB)
USION)		40	SRC PHYSPROP
ROCHLORIDE)			
co-adminsitered CILASTATIN SODIUM)			
ROCHLORIDE EXTENDED RELEASE)		94-95	SRC PHYSPROP
		213.5	SRC PHYSPROP
		70	SRC PHYSPROP
		88	Chemfinder DEMO PerkinElmer Imformat

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			174.5	Hazardous Substances Data Bank (HSDB)
LFATE)			182	Hazardous Substances Data Bank (HSDB)
			143	http://www.ema.europa.eu/docs/en_GB,
Carrier med http://www	E			
			230	Chemfinder DEMO PerkinElmer Imformat
			117	Hazardous Substances Data Bank (HSDB)
Carrier med Knox C, Law	E	Weak affinity		
.EATE)			117	AQUASOL dATAbASE 6th edition
			240	SRC PHYSPROP
IUM SALT)			236.5	SRC PHYSPROP
AS TROMETHAMINE)				
			88-90	SRC PHYSPROP
			206	SRC PHYSPROP
			113	Chemfinder DEMO PerkinElmer Imformat
ministered with an oestrogen)			159	SRC PHYSPROP
ROCHLORIDE)			35.5	SRC PHYSPROP
			257	SRC PHYSPROP
			215	Hazardous Substances Data Bank (HSDB)
ROCHLORIDE)			270	SRC PHYSPROP
			313	SRC PHYSPROP
ECTION)				
			240	http://www.baxter.ca/en/downloads/prc
inistered NORETHYNODREL)			150.5	SRC PHYSPROP
			93	SRC PHYSPROP
			52.5	SRC PHYSPROP
.EATE)			172	SRC PHYSPROP
			50.5	SRC PHYSPROP
SODIUM)				
ROCHLORIDE)			283	Hazardous Substances Data Bank (HSDB)
			150	Hazardous Substances Data Bank (HSDB)
			114	Hazardous Substances Data Bank (HSDB)
			>300	SRC PHYSPROP
			77	SRC PHYSPROP
JECTION CHLORIDE)				
			165	Hazardous Substances Data Bank (HSDB)
Carrier med Knox C, Law	I	Medium to weak affinity		
			140.5	SRC PHYSPROP
Carrier Med Mougey EB,	I			
			156.5	SRC PHYSPROP
USION)				
ROCHLORIDE)			208.5	Hazardous Substances Data Bank (HSDB)
ROCHLORIDE)			144.5	SRC PHYSPROP
			93.5	Hazardous Substances Data Bank (HSDB)

LATE)				
ROCHLORIDE)				
			172	Li G, Su GQ, Xu QW., et al., Yao Xue Xue B
			299	SRC PHYSPROP
ROCHLORIDE)			83.5	SRC PHYSPROP
ROCHLORIDE)				
FATE)				
FUSION AS SULFATE)				
ed release)			236.6	SRC PHYSPROP
			92.5	SRC PHYSPROP
g release)				
ed release)				
ug reference, Ed 36th, Sweetman, SC., Pharmaceutical			180	SRC PHYSPROP
Carrier med Knox C, Law	E		131	SRC PHYSPROP
			180	SRC PHYSPROP
Carrier med Knox C, Law	E		216	SRC PHYSPROP
			43	Hazardous Substances Data Bank (HSDB)
			148	SRC PHYSPROP
			153.6	SRC PHYSPROP
			215.5	SRC PHYSPROP
MIDE)				
			96	SRC PHYSPROP
YDRATE)			184.5	SRC PHYSPROP
MIDE IV)			215	Hazardous Substances Data Bank (HSDB)
IUM)			139.5	Hazardous Substances Data Bank (HSDB)
FATE)			130.5	MSDS Sigma aldrich http://www.sigmaalc
			146.3	SRC PHYSPROP
DIUM)			129.5	SRC PHYSPROP
ed release)			105	Chemfinder DEMO PerkinElmer Imformat
eate)				
Carrier med Knox C, Law	I	Medium to low affinity		
			215	SRC PHYSPROP
			126	SRC PHYSPROP
			150	SRC PHYSPROP
			179.5	SRC PHYSPROP
			72	SRC PHYSPROP
ROCHLORIDE)			101.25	Hazardous Substances Data Bank (HSDB)
			273	SRC PHYSPROP
			105.5	SRC PHYSPROP
EATE)				
			214	SRC PHYSPROP
USION AS CHLORIDE)				
			281.5	SRC PHYSPROP
			195	SRC PHYSPROP

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			125	SRC PHYSPROP
FUSION AS HYDROCHLORIDE)			167	Hazardous Substances Data Bank (HSDB)
ROCHLORIDE)			224.5	Hazardous Substances Data Bank (HSDB)
Carrier med May K, Gies	E			
			136.7	SRC PHYSPROP
ROCHLORIDE)			170	Hazardous Substances Data Bank (HSDB)
			135.5	SRC PHYSPROP
			192	SRC PHYSPROP
			233.5	SRC PHYSPROP
ROCHLORIDE)				
IUM)			100	SRC PHYSPROP
Carrier med Knütter I, W	I	Low affinity fo	120	Hazardous Substances Data Bank (HSDB)
IUM)			99.5	Hazardous Substances Data Bank (HSDB)
Carrier med Knox C, Law	I	Medium to lov	109	SRC PHYSPROP
			203.5	SRC PHYSPROP
ROCHLORIDE)				
ZOATE)				
			228	SRC PHYSPROP
FATE)			151	SRC PHYSPROP
			147	SRC PHYSPROP
ROCHLORIDE)				
			194.25	Hazardous Substances Data Bank (HSDB),
Carrier med Yamaguchi I	E			
Carrier med Knox C, Law	E			
CINATE)				
Carrier med Knox C, Law	I	Medium to low affinity		
IECTION SULFATE)				
ECTION/INFUSION)			115	SRC PHYSPROP
			193.5	SRC PHYSPROP
USION)			97	SRC PHYSPROP
administered with AMPICILLIN SODIUM INFUSION)				
inistered as SULFADIAZINE;SULFAMERAZINE)			198.5	SRC PHYSPROP
			136.5	SRC PHYSPROP
			243	SRC PHYSPROP
			181.5	SRC PHYSPROP
			124.3	SRC PHYSPROP
Carrier med Buxbaum E.,	E			
ROCHLORIDE)			229	Hazardous Substances Data Bank (HSDB)
ROCHLORIDE)				
ECTION)				
			120	SRC PHYSPROP
ROCHLORIDE)			< 25	SRC PHYSPROP
			300	SRC PHYSPROP
			73	SRC PHYSPROP
			167	SRC PHYSPROP
USION co administered with Clavulanic acid AS SODIUM)				
ROCHLORIDE)				
ROCHLORIDE)				
ROCHLORIDE)				

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.ATION)				
ROCHLORIDE)			256	SRC PHYSPROP
INJECTION HYDROCHLORIDE)			174	SRC PHYSPROP
TRATE)				
Carrier med Knox C, Law	E			
Carrier med Knox C, Law	I	Medium to low affinity		
			100	SRC PHYSPROP
			270	SRC PHYSPROP
ECTION)			293	SRC PHYSPROP
ROCHLORIDE)			232	SRC PHYSPROP
ROCHLORIDE)			114	Hazardous Substances Data Bank (HSDB)
TRATE)			68	SRC PHYSPROP
			50.5	SRC PHYSPROP
ECTION AS CHLORIDE)			269	Hazardous Substances Data Bank (HSDB)
			157	SRC PHYSPROP
DROCHLORIDE)				
TRATE)				
Carrier med Balayssac D,	E		228	SRC PHYSPROP
Carrier Med Abbot EL, Gr	I			
			63.5	SRC PHYSPROP
)			3	SRC PHYSPROP
			178	SRC PHYSPROP
			256	SRC PHYSPROP
Carrier med Estudante M	I		217.5	SRC PHYSPROP
tion)			256	Hazardous Substances Data Bank (HSDB)
			178	SRC PHYSPROP
			133.5	MSDS Sigma aldrich http://www.sigmaalc
			200	SRC PHYSPROP
			105.5	SRC PHYSPROP
			174.5	MSDS http://www.sciencelab.com/msds.
			158	SRC PHYSPROP
			166.5	SRC PHYSPROP
			166.5	Hazardous Substances Data Bank (HSDB)
DROCHLORIDE)			188.7	SRC PHYSPROP
ed release)				
administered SULFADIAZINE)			236	SRC PHYSPROP
			239	SRC PHYSPROP
			96	SRC PHYSPROP
COPHENOLATE SODIUM)			141	SRC PHYSPROP
ROCHLORIDE)				
ROCHLORIDE)			183.5	Hazardous Substances Data Bank (HSDB)
			120.5	SRC PHYSPROP
YLATE)			227	Hazardous Substances Data Bank (HSDB)
DROCHLORIDE)			141	Chemfinder DEMO PerkinElmer Imformat
			179.5	SRC PHYSPROP
			61	SRC PHYSPROP

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Carrier med Knox C, Law	E	117.25	Hazardous Substances Data Bank (HSDB)
Carrier med Uchino H, Ka	I		
USION AS SODIUM)		192	MSDS http://www.sciencelab.com/msds.
		188	SRC PHYSPROP
		161	SRC PHYSPROP
ROCHLORIDE)		127	SRC PHYSPROP
		76	SRC PHYSPROP
)TASSIUM)			
/ DJ, et al., Epilepsia. 1982 Jun;23(3):307-13		120	Chemfinder DEMO PerkinElmer Imformat
		138	Hazardous Substances Data Bank (HSDB)
		228.5	SRC PHYSPROP
		198.5	Hazardous Substances Data Bank (HSDB)
Carrier med Tsuda M, Te	I	150	Hazardous Substances Data Bank (HSDB)
		254	SRC PHYSPROP
		219	MSDS Sigma aldrich http://www.sigmaalc
		285	SRC PHYSPROP
/DROCHLORIDE)			
		236.5	SRC PHYSPROP
DROCHLORIDE)			
		116.2	SRC PHYSPROP
ROCHLORIDE)			
FUSION)		160.5	Hazardous Substances Data Bank (HSDB),
		175	SRC PHYSPROP
		113	SRC PHYSPROP
ıl dosing)		119	SRC PHYSPROP
ed release)			
		203	SRC PHYSPROP
olet 100-250mg/kg daily in 2-4 divdied doses			
Carrier med http://www	E		
		128	SRC PHYSPROP
		173	Hazardous Substances Data Bank (HSDB)
ECTION)		156	SRC PHYSPROP
		224.5	SRC PHYSPROP
ORIDE)			
CONATE)		134	SRC PHYSPROP
		>300	Hazardous Substances Data Bank (HSDB)
		245	SRC PHYSPROP
, IV), Solution (equivalent to 350 mg I per mL)		177	SRC PHYSPROP
USION AS MEGLUMINE)			
USION AS MEGLUMINE)			
BROMIDE)			
USION)		220	SRC PHYSPROP
JM IV)		227	Hazardous Substances Data Bank (HSDB)
MIDE)		160	Hazardous Substances Data Bank (HSDB)
ACETATE)			

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tics database; Accessed 22Apr2013-6May2013

(Beta-Naphthalensulfonate Trihydrate)

sh/out/0471755.20070104.7029.pdf

(Monohydrate)

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tics database; Accessed 22Apr2013-6May2013

et al., Proc Natl Acad Sci U S A. 2003 Mar 4;100(5):2180-4

(Hydrochloride monohydrate)

(under nitrogen)

(Hydrobromide)

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(Hydrochloride)

roducts/monograph/273

(0.4 H2O)

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p 1;13(17):5001-12

(Sodium)

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‹pert Opin Pharmacother. 2013 May;14(7):905-16

Methanesulfonate
/files/pdf/product_monograph/Fluanxo_MKT_PM_ctrl148918_18OCT2011_eng.pdf

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Methanesulfonate

Asian J. Pharm, 2008, 2(2) 96-101

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tics database; Accessed 22Apr2013-6May2013, (hydrochloride)

(Bromide)

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(Hydrogen sulfate)

(Hydrochloride)
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drich.com

p 1;13(17):5001-12

(Sulfate)

tics database; Accessed 22Apr2013-6May2013

tics database; Accessed 22Apr2013-6May2013

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/document_library/Application_withdrawal_assessment_report/2010/01/WC500064326.pdf

tics database; Accessed 22Apr2013-6May2013, Hydrochloride

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ao. 2001 Jul;36(7):532-4

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hydrochloride monohydrate

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tics database; Accessed 22Apr2013-6May2013

drich.com

(Monohydrate)

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Supporting information - Outliers from Figure 1

Outlier type	Name	Therapeutic indication/Class	Transport Route	Comments	References
Higher permeability in caco-2 compared to MDCK	Oseltamivir	Antiviral	Influx, PEPT1 & Efflux, P-gp	PEPT1 is not detected in MDCK cells;therefore higher permeability for the caco-2 cell lines	Ogihara, T.; Kano, T.; Wagatsuma, T.; Wada, S.; Yabuuchi, H.; Enomoto, S.; Morimoto, K.; Shirasaka, Y.; Kobayashi, S.; Tamai, I., Oseltamivir (Tamiflu) Is a Substrate of Peptide Transporter 1
	Loperamide	Opioid/gastrointestinal	Efflux, P-gp	In this case the MDCK permeability is lower compared to caco-2 permeability due to the strain of MDCK used which over expresses the p-gp transporter therefore would expect lower permeability in MDCK-MDR1 cells compared to caco-2	Varma, M. V. S.; Sateesh, K.; Panchagnula, R., Functional role of P-glycoprotein in limiting intestinal absorption of drugs: Contribution of passive permeability to P-glycoprotein mediated efflux transport. Molecular Pharmaceutics 2005, 2, 12-21. Troutman, M. D.; Thakker, D. R., Novel experimental parameters to quantify the modulation of absorptive and secretory transport of compounds by P-glycoprotein in cell culture models of intestinal epithelium. Pharmaceutical Research 2003, 20, 1210-1224.
	Amitriptyline	Antidepressant	Efflux, P-gp	In this case the MDCK permeability is lower compared to caco-2 permeability due to the strain of MDCK used which over expresses the p-gp transporter therefore would expect lower permeability in MDCK-MDR1 cells compared to caco-2	Faassen, F.; Vogel, G.; Spanings, H.; Vromans, H., Caco-2 permeability, P-glycoprotein transport ratios and brain penetration of heterocyclic drugs. International Journal of Pharmaceutics 2003, 263, 113-122. Troutman, M. D.; Thakker, D. R., Novel experimental parameters to quantify the modulation of absorptive and secretory transport of compounds by P-glycoprotein in cell culture models of intestinal epithelium. Pharmaceutical Research 2003, 20, 1210-1224.
	Phenazopyridine	Analgesic	Passive Transcellular	Poor solubility (dissolution limiting) - BCS class 2 compound	Gao, Z., Development of a Continuous Dissolution/Absorption System—a Technical Note. AAPS PharmSciTech 2012, 13, 1287-1292.
Higher permeability in MDCK compared to caco-2	Sotalol	Antiarrhythmic	Paracellular & influx transporter OATP-A	OATP-A is expressed in caco-2 but not determined in MDCK II. In addition MDCK II cells are leakier compared with caco-2 hence both reasons could contribute to higher absorption through the MDCK cell line	Liu, W. et al, Sotalol Permeability in Cultured-Cell, Rat Intestine, and PAMPA System. Pharmaceutical Research 2012, 29, 1768-1774.
	Dicloxacillin	Antibiotic	Influx, PEPT1 & Efflux, P-gp	Higher expression of p-gp in caco-2 and higher efflux of dicloxacillin by this transporter than uptake by PEPT1 could explain higher permeability in MDCK cell line.	Luckner, P.; Brandsch, M., Interaction of 31 β-lactam antibiotics with the H+/peptide symporter PEPT2: analysis of affinity constants and comparison with PEPT1. European Journal of Pharmaceutics and Biopharmaceutics 2005, 59, 17-24. Susanto M, Benet LZ. Can the enhanced renal clearance of antibiotics in cystic fibrosis patients be explained by P-glycoprotein transport? Pharm Res. 2002 Apr;19(4):457-62.
	Levodopa	Psychoactive	Influx, LNAA	Higher abundance of LNAA in MDCK cells compared with caco-2, in addition the possibility of paracellular absorption has been proposed and based on the MDCK cell line which is leakier both could explain the higher permeability in MDCK compared to caco-2	Putnam, W. S.; Ramanathan, S.; Pan, L.; Takahashi, L. H.; Benet, L. Z., Functional characterization of monocarboxylic acid, large neutral amino acid, bile acid and peptide transporters, and P-glycoprotein in MDCK and Caco-2 cells. Journal of Pharmaceutical Sciences 2002, 91, 2622-2635. Lennernas, H.; Nilsson, D.; Aquilonius, S. M.; Ahrenstedt, O.; Knutson, L.; Paalzow, L. K., The effect of L-leucine on the absorption of levodopa, studies by regional jejunal perfusion in man. British Journal of Clinical Pharmacology 1993, 35, 243-250.
	Sildenafil	Erectile dysfunction and pulmonary arterial hypertension	Efflux, P-gp & BCRP	BCRP transporter was not determined in MDCK II cells indicating that the combined efflux effect of p-gp and BCRP transporters in caco-2 reduce the permeability more compared to the single efflux transporter in the MDCK cell line hence the higher permeability in the MDCK cell line	Choi, M. K.; Song, I. S., Characterization of efflux transport of the PDE5 inhibitors, vardenafil and sildenafil. Journal of Pharmacy and Pharmacology 2012, 64, 1074-1083. Di, L.; Whitney-Pickett, C.; Umland, J. P.; Zhang, H.; Zhang, X.; Gebhard, D. F.; Lai, Y. R.; Federico, J. J.; Davidson, R. E.; Smith, R.; Reyner, E. L.; Lee, C.; Feng, B.; Rotter, C.; Varma, M. V.; Kempshall, S.; Fenner, K.; El-Kattan, A. F.; Liston, T. E.; Troutman, M. D., Development of a New Permeability Assay Using Low-Efflux MDCKII Cells. Journal of Pharmaceutical Sciences 2011, 100, 4974-4985.
	Glipizide	Anti-diabetic	Passive Transcellular	Poor solubility (dissolution limiting) - BCS class 2 compound	Mehramizi, A.; Alijani, B.; Pourfarzib, M.; Dorkoosh, F. A.; Rafiee – Tehrani, M., Solid Carriers for Improved Solubility of Glipizide in Osmotically Controlled Oral Drug Delivery System. Drug Development and Industrial Pharmacy 2007, 33, 812-823.

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Supporting Information III

Table S1. Comparison of small intestine and *in vitro* cell lines; 'y' indicates transporter and enzyme expression; Bold text indicates high expression; italic indicates moderate, normal text indicates low expression according to the literature

Cell line	**Small intestine**	**Caco-2**	**MDCK**	**Refs**
Species	Human	Human	Canine	[1, 2]
Tissue	Small intestine	Colon adenocarcinoma	Kidney	[1, 2]
Culture time (days)	N/A	21[a]	3-5	[1, 2]
TEER ($\Omega.cm^2$)	25-40	300-500	Parental MDCK <200 MDCK I >1000 MDCK II <300 MDCK-MDR1 1000-10000	[1-9]
Unstirred water layer (UWL) thickness (µm)	<100	1000-2500	NF	[10-13]
Transporter expression	Transporter expression is highest in small intestine (area dependent) compared to cell lines in most cases. Transport expression is lower in MDCK cells compared to Caco-2 cells[4]			
MDR1(P-gp)	*y*	*y*	y y MDCK II *y* MDCK-MDR1	[4, 6, 14-19]
MDR3	y	y	y MDCK II	[6, 18, 20]
HPT1	**y**	**y**	NF	[18, 20-22]
PEPT1	**y**	*y*	ND MDCK II	[6, 15-18, 20, 22, 23]
PEPT2	ND	ND	y MDCK II	[6, 15, 18, 20, 24]
OCTN1	y	y	NF	[17, 18, 20, 22]
OCTN2	*y*	y	NF	[1, 16-18, 20]
MCT1	*y*	*y*	y MDCK II	[16, 17, 20, 25]
MCT2	ND	y	NF	[26-28]
MCT3	y	y	ND MDCK II	[18, 22, 25]
MCT4	y	*y*	y MDCK II	[18, 25-27, 29]
MCT5	*y*	y	NF	[18, 20]
IBAT	*y*	*y*	NF	[5, 18, 20]
OAT1	ND	ND	ND MDCK II	[6, 16, 18, 20, 30]
OAT2	y	y	NF	[16, 20]
OAT3	ND	ND	NF	[18, 20]
OAT4	ND	y	NF	[18, 20, 31]
OATP-A	y	y	ND MDCK II	[6, 17, 20, 32, 33]
OATP-B	y	**y**	NF	[16-18, 23, 32]
OATP-C	ND	ND	ND MDCK II ND*	[18, 20, 33]
OATP-D	y	y	NF	[18, 20, 34]
OATP-E	y	y	NF	[18, 20, 34]
OATP-F	y	ND	NF	[18, 20]

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OATP-H	y	y	ND* ND MDCK II	18, 20, 35, 36
OATP8	y	ND	ND MDCK II	6, 18, 20, 32
BCRP	**y**	*y*	ND* ND MDCK II	6, 14, 16-19, 23, 37
MRP1	y	y	y* y MDCK II y MDCK-MDR1	14, 17-20, 33
MRP2	**y**	**y**	ND* y MDCK II y MDCK-MDR1	6, 14, 16-18, 20, 23, 33
MRP3	*y*	*y*	y MDCK II	6, 16, 17, 20
MRP5	y	y	y MDCK II y MDCK-MDR1	6, 14, 19, 20, 22
MRP6	y	y	NF	17
OCT1	y	y	NF	16-18, 20
OCT2	ND	ND	y MDCK II	6, 18, 20, 38
OCT3	y	y	ND MDCK II	6, 16-18
ENT1	y	y	y MDCK II	6, 18, 22, 39
LNAA (LAT1/LAT2)	y	y	y*	5, 40
PHT1	y	y	y MDCK II	6, 41
LRP	*y*	NF	NF	20, 42
Cycloph A	**y**	NF	NF	20
CNT3	ND	*y*	ND*	18, 20, 43
Enzyme expression	Enzymes expressed in the small intestine have higher abundance compared to the cell lines.			
CYP3A4	**y**	y (very low)	ND*	4, 22, 44-46
CYP2D6	y	y (very low)	NF	18, 44, 45
CYP2C9	**y**	*y*	NF	18, 22, 44, 45
CYP2C19	*y*	*y*	NF	18, 22, 44, 45
CYP1A1	y	y	NF	44, 45
CYP2J2	*y*	y	ND MDCK II	6, 22, 44, 45
CYP3A5	y	y	NF	18, 44, 45
UGT	y	y	NF	22
GST	y	y	y*	1, 22, 47
ST	y	y	y MDCK II	1, 22, 48
AT	y	y	NF	22
AcyT	y	y	NF	22

[a]when P-gp expression is at its maximum[4]; NF- not found in the literature; ND - not detected in experimental assay; MDR - multi drug resistant protein; HPT1 - human oligopeptide transporter; PEPT- peptide transporter; OCTN - organic cation transporter; MCT- monocarboxylate transporters; IBAT - ileal sodium-dependent bile acid transporter/ intestinal bile acid transporter; OAT - organic anion transporter; OATP - Organic anion-transporting polypeptide; BCRP - Breast cancer resistance protein; MRP - multidrug resistance associated protein; OCT - organic cation transporter; ENT - equilibrative nucleoside transporter; LNAA/ LAT - Large neutral amino acids; LRP - lipoprotein transporter; Cycloph A - cyclophilin A/ Peptidyl-prolyl Isomerase A, CNT - Concentrative nucleoside transporter; CYP - Cytochrome P450 enzyme; UGT- Uridine 5'-diphospho-glucuronosyltransferase; GST - glutathione S-transferase; ST- sulfotransferase; AT - N-acetyltransferase; AcyT – acyltrtransferase

*Note: A generic term MDCK is used unless specific information regarding the transporter in a specific strain is known. Therefore MDCK could indicate that the parietal MDCK has been used or that the strain was not specified in the study

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Comparison of absorption through MDCK and Caco-2 cell lines using different mechanisms/ routes

The statistical significance of the regression lines (slope and intercept) of the absorption mechanisms highlighted in **Table 3 (in manuscript)** was tested and the results are shown in **Table S2**. As some of the compounds undergo more than one absorption mechanism (Groups D, F, G and H in **Table 3**), the significance was also tested in either mechanism. For example, for group D (efflux and paracellular) this was tested with all these compounds classed as efflux or classed as paracellular. P values < 0.05 indicate that there is a significant difference between the intercept and slope of the lines of the absorption groups being studied.

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Table S2. Linear regression results and significance of the different absorption transport routes (First absorption mechanism is dominant for that set)

Model	Description	N	Slope	Slope p value	Intercept	Intercept p value
1*	Paracellular (B, D ,F ,H) Vs Transcellular (A)	11 83	-0.191 -0.874	0.0023**	-7.370 -0.688	n/a
2	Carrier mediated (C-H) Vs Passive (A, B)	96 89	0.777 0.880	0.297	-1.239 -0.663	0.525
3	Efflux (C, D, G, H) Vs Passive (A, B)	79 89	0.787 0.880	0.355	-1.194 -0.663	0.479
4	Influx (E, F, G, H) Vs Passive (A, B)	32 89	0.673 0.880	0.132	-1.899 -0.663	0.326
5	Efflux (C, D, G, H) Vs Influx (E, F)	79 17	0.787 0.750	0.867	-1.194 -1.376	0.895
6	Influx (E, F, G, H) Vs Efflux (C, D)	32 64	0.673 0.795	0.498	-1.899 -1.113	0.338
7	Influx (E, F) Vs Efflux (C, D)	17 64	0.750 0.795	0.844	-1.376 -1.113	0.915

* Paired t tests were carried out on the smaller group of permeability values to test the significance between the two cell lines of the group of compounds. In addition paired t tests were also carried out for all the groups in models 1-7 to test for significance between the cell lines. All tests revealed not significant differences between the two cell lines.

**indicates statistical significance between the groups

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Table S3. Molecular descriptors utilised in 12 models from Table 6 in manuscript

Descriptor	**Description**	**Model used (1-12) from Table 6**
ABSQ	Sum of absolute values of atomic partial charges of the molecule	2,8,9,10
ACD_PSA	Polar Surface Area	2,3,4,5,6,7,9
Balaban Topological Index	Highly discriminant topological descriptor, gives an indication of shape including branching and cyclicity of a molecule	1,3,4,7,8,10,11,12
Dipole	Measure of polarity plus other internal electronic effects of the molecules	2,5,9
GSE solubility	Aqueous solubility calculated using the general solubility equation	3,5,7,10,11
Hmin	Minimum hydrogen EState value in molecule	2,5,9
Inertia Moment 2 Length	Indicates the strength and orientation behaviors of molecule in an electrostatic field.	6
logDN	logarithm of dose number	6
LogP	Octanol/water partition coefficient	1,11,12
logPapp	logarithm of cell apparent permeability (cm/s^{-1})	1-12
logS (M)	logarithm of experimental aqueous solubility in Molar units (M)	8,9,10
LogS (mg/mL)	logarithm of experimental aqueous solubility in mg/mL	2,5,9
Max Neg	Largest negative charge over the atoms in the compound	1
MPbAP	Melting Point based Absorption Potential	4,6,7,8,12
Phia	Kappa flexibility index	1
Qv	Molecular and group polarity index	1
SHHBd	Sum of the hydrogen atom level E-state values for all hydrogen atoms bonded to donating atoms.	1,11,12
SsCH3	Sum of all (-CH3 -) E-state values in molecule	1,11,12
VAMP HOMO	Energy of the highest occupied molecular orbital calculated by AM1 semi empirical method	1,11,12
VAMP LUMO	Energy of the lowest unoccupied molecular orbital calculated by AM1 semi empirical method	2,5,6,9

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Figures showing the relationship between the different transport mechanisms between the 185 compounds for caco-2 and MDCK permeability

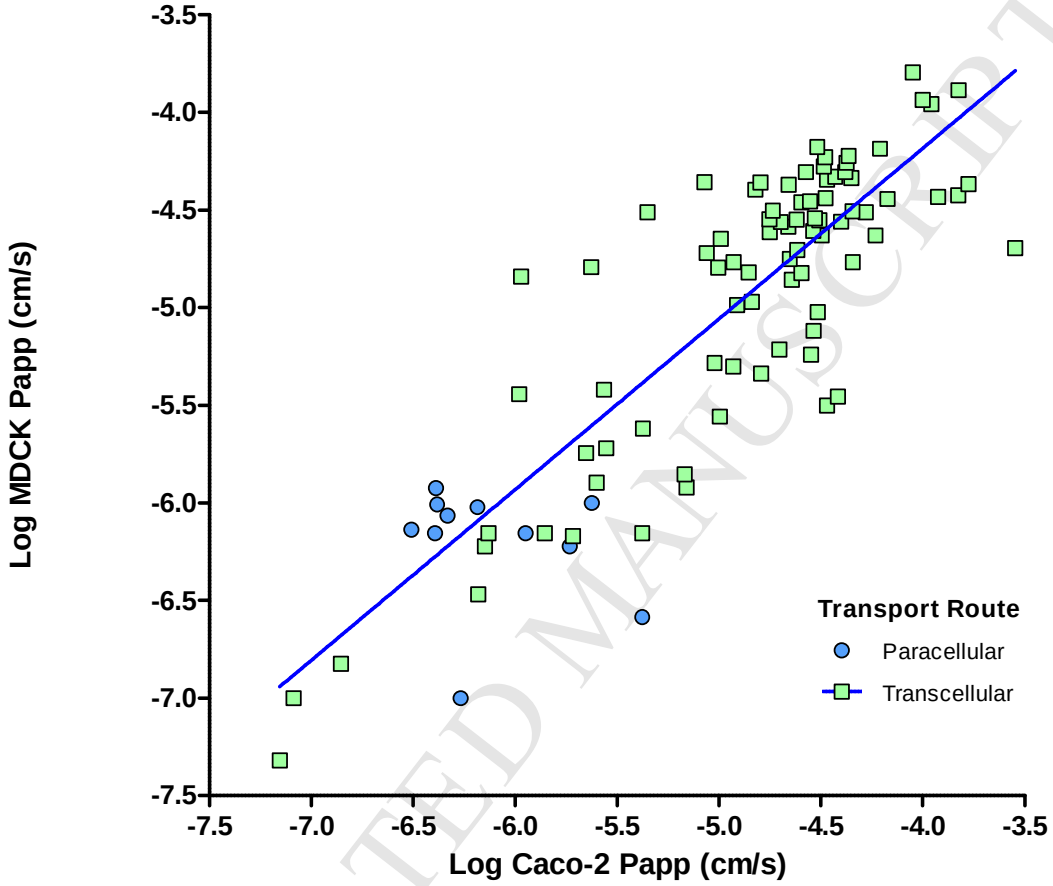

Figure S1. Comparison of regression between compounds transcellular and paracellular (model 1).

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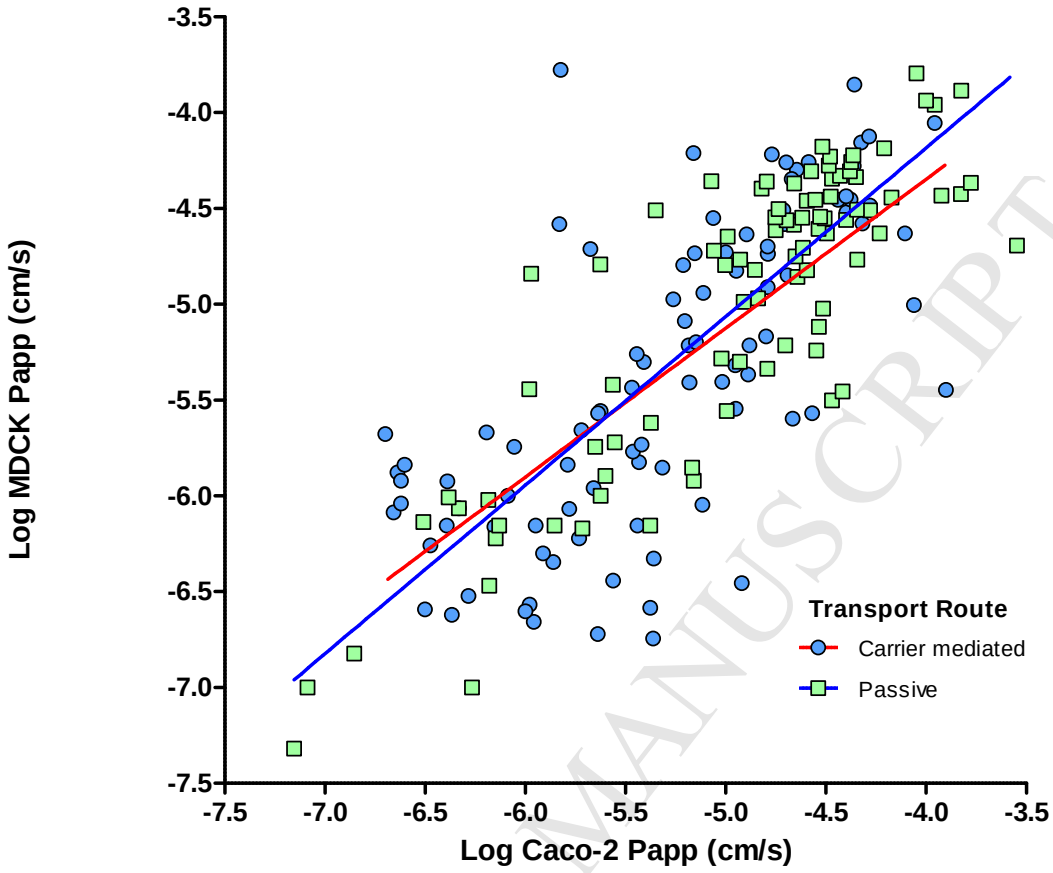

Figure S2. Comparison of regression between carrier mediated transport and passive absorption compounds (model 2)

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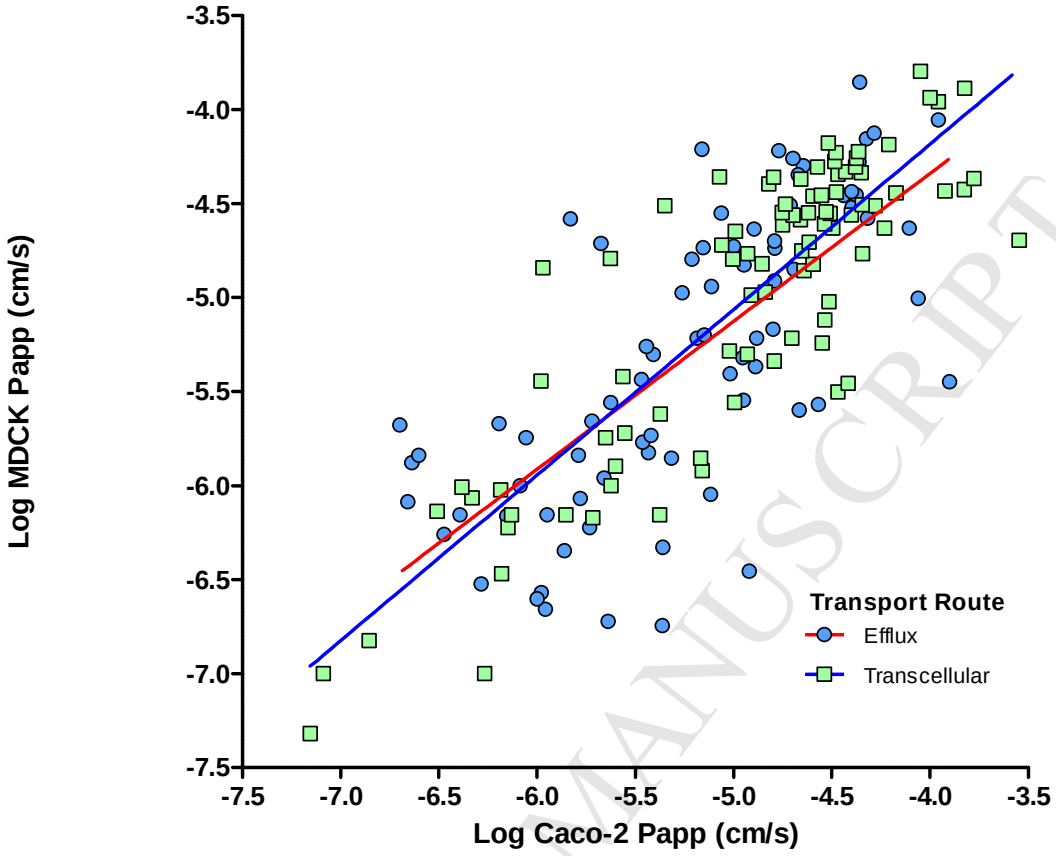

Figure S3. Comparison of regression between compounds identified as carrier mediated efflux transport and passive absorption (model 3)

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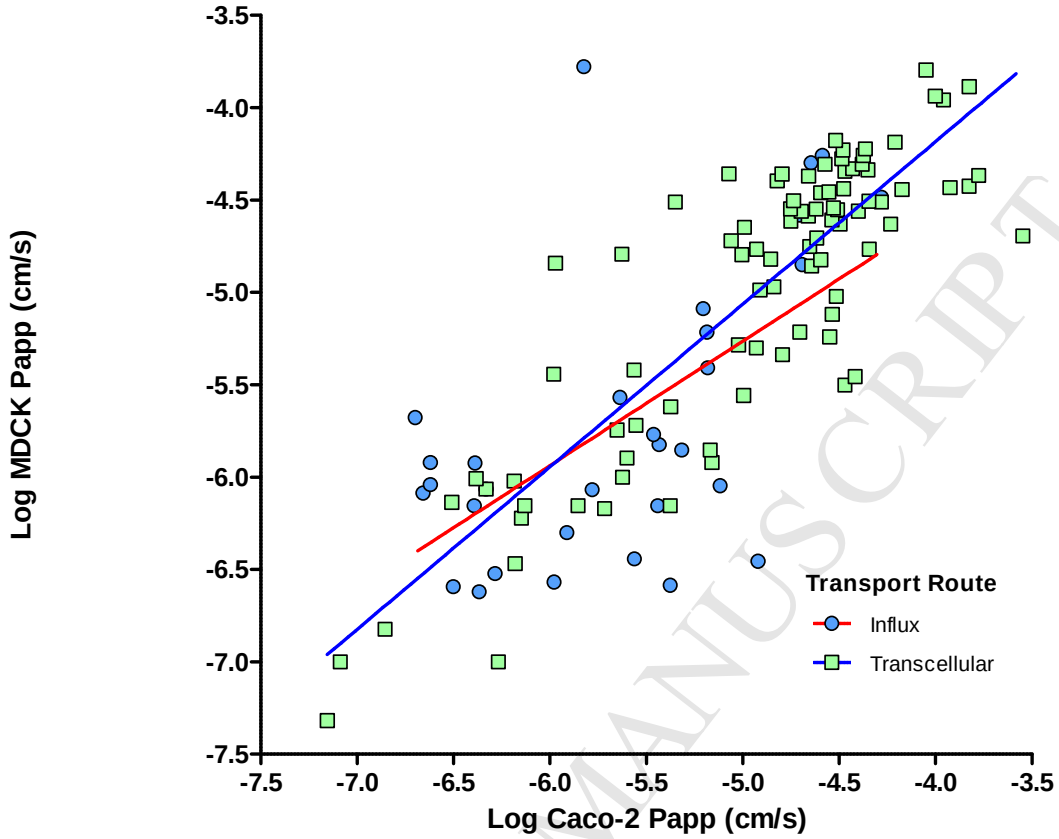

Figure S4. Comparison of regression between compounds identified as carrier mediated influx transport and passive absorption (model 4)

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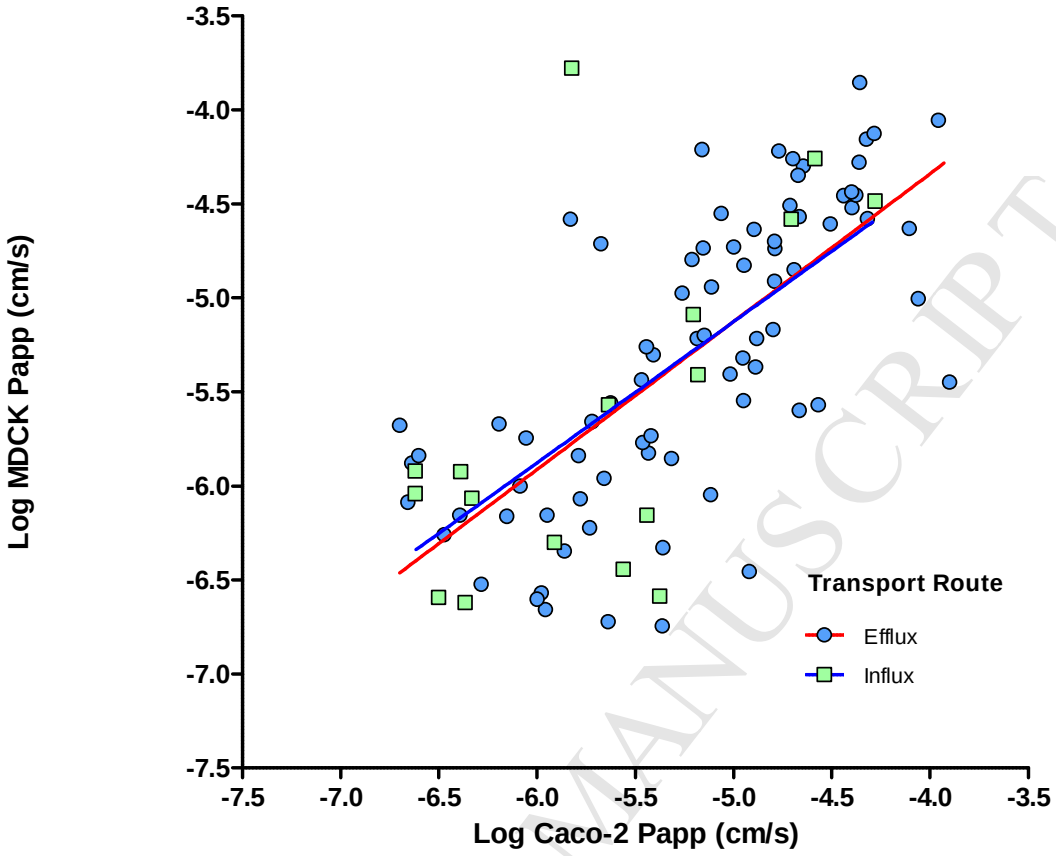

Figure S5. Comparison of regression between carrier mediated efflux and influx transport (model 5)

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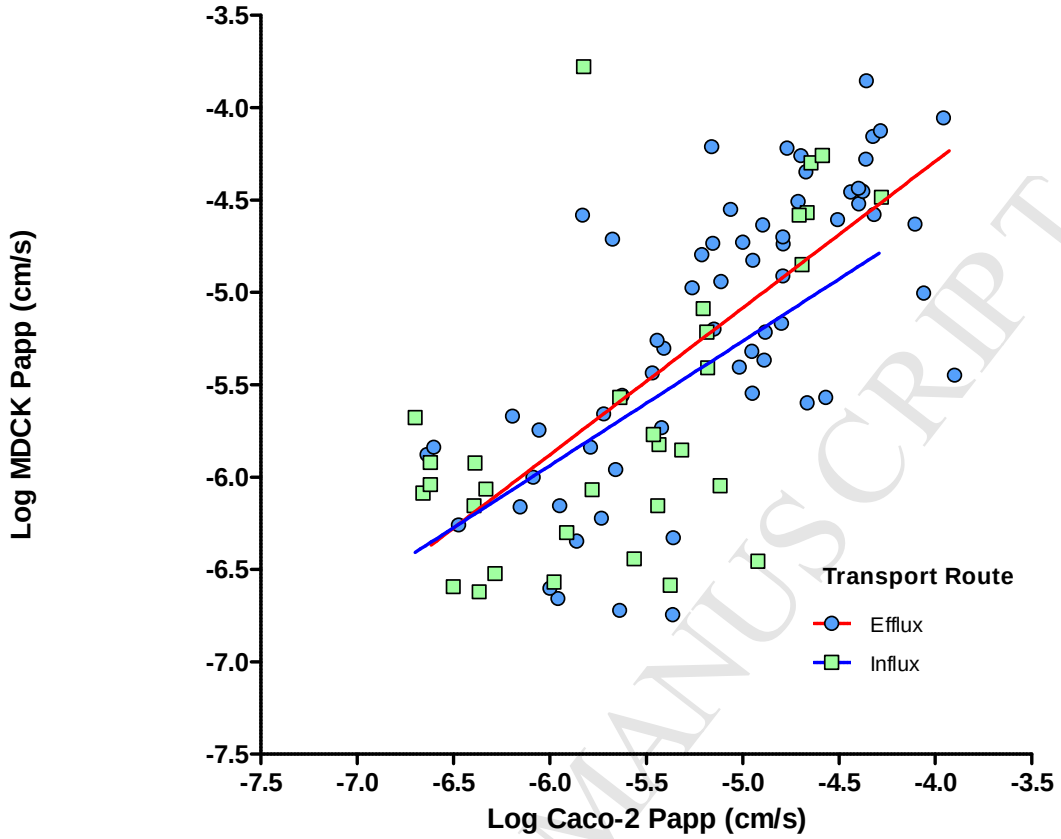

Figure S6. Comparison of regression between carrier mediated efflux and influx transport (groups C-F **Table 3**) Model 6

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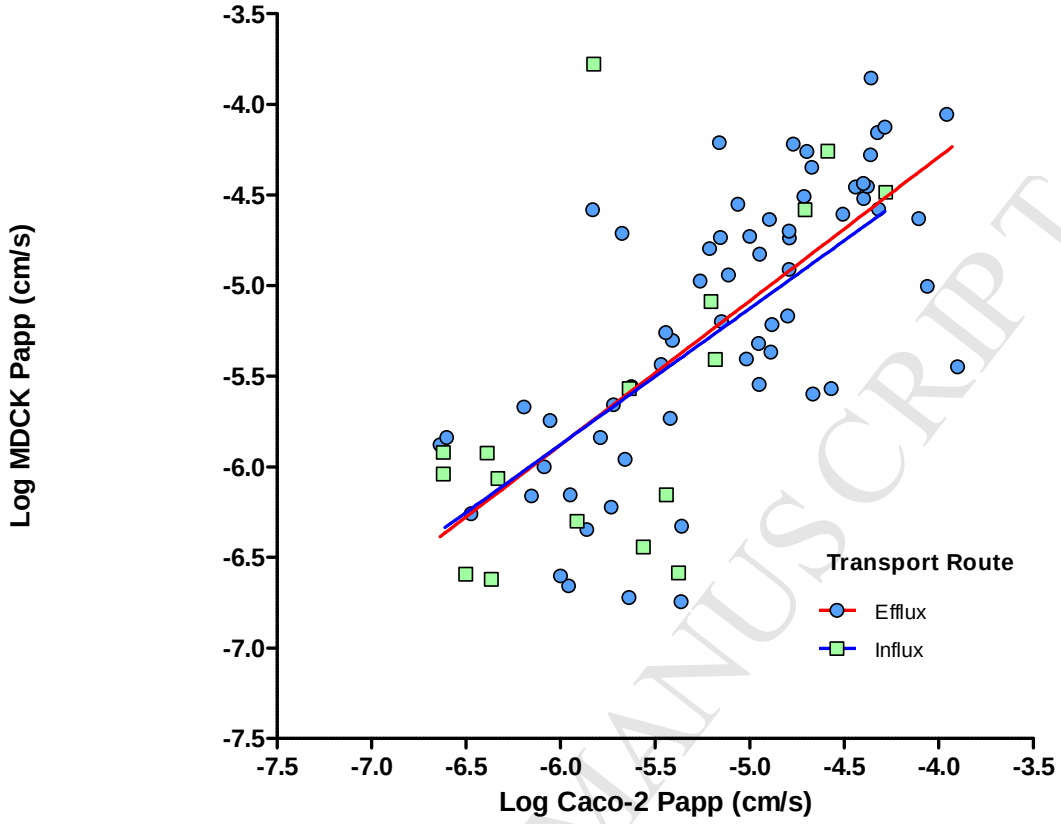

Figure S7. Comparison of regression between carrier mediated influx (groups E, F **Table 3**) and efflux transport (groups C,D **Table 3**) Model 7

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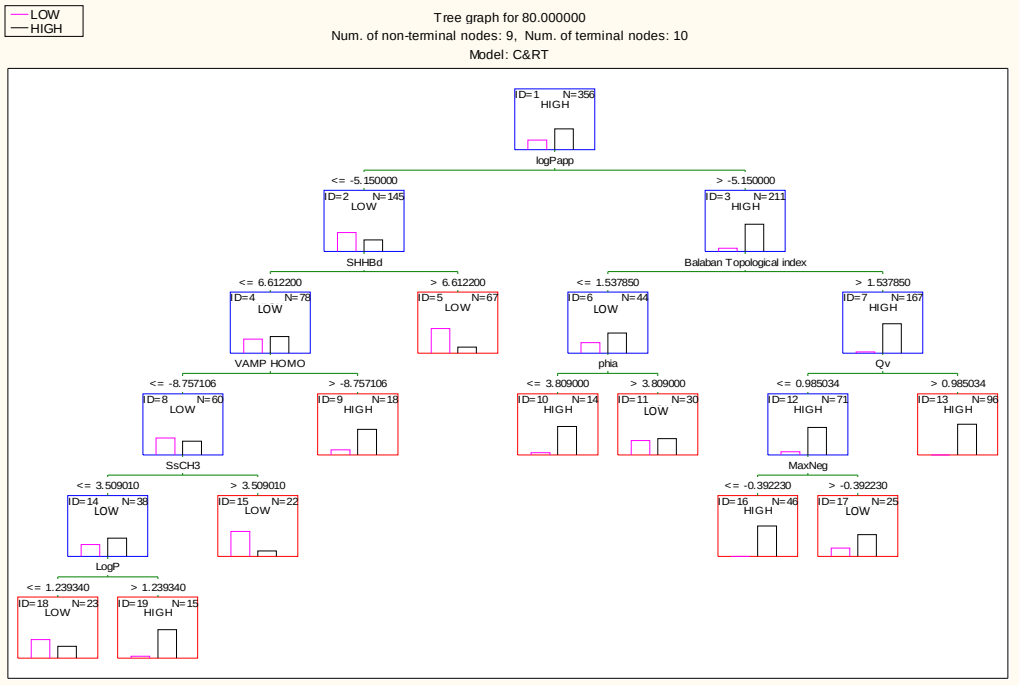
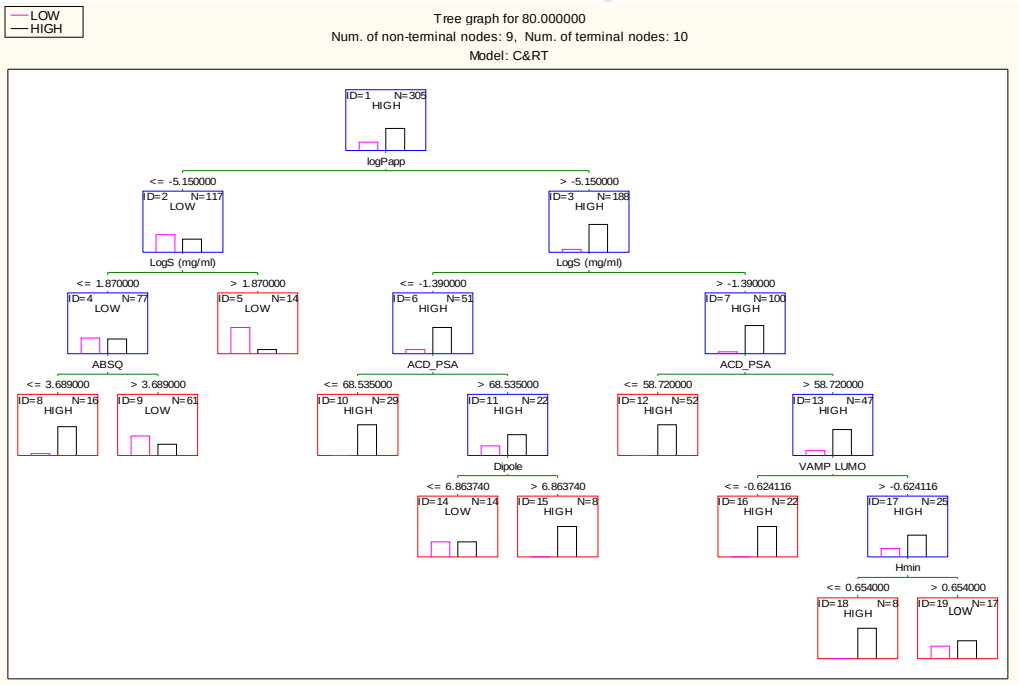
12 C&RT models from **Table 7** from manuscript

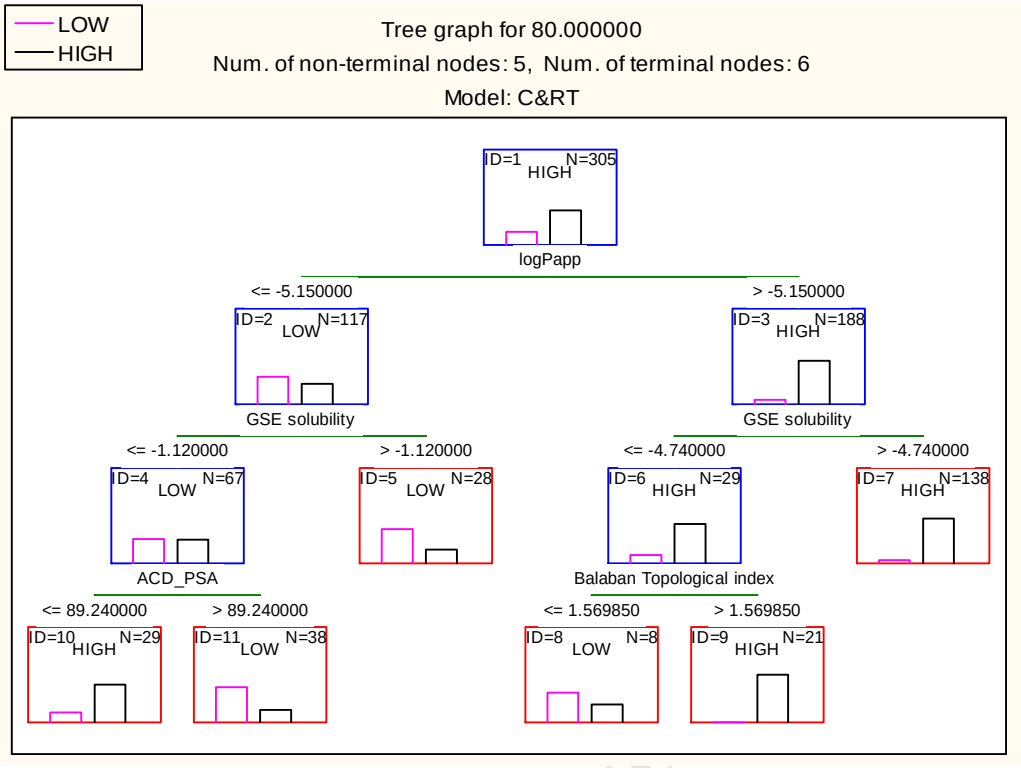
Model 1



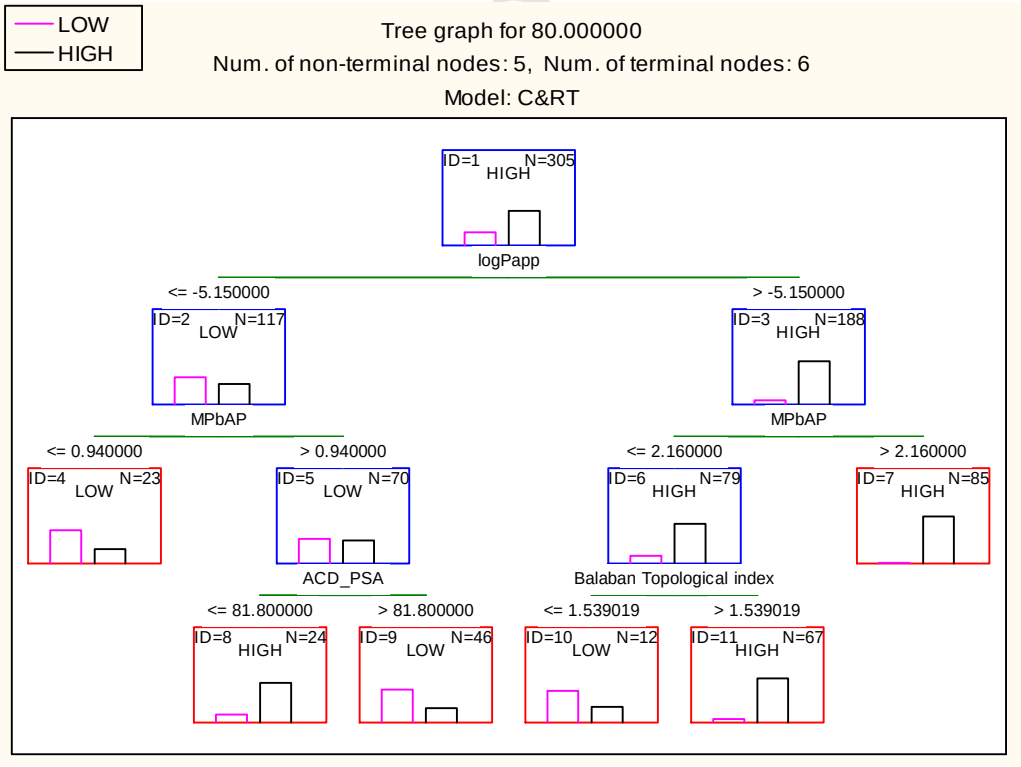
Model 2



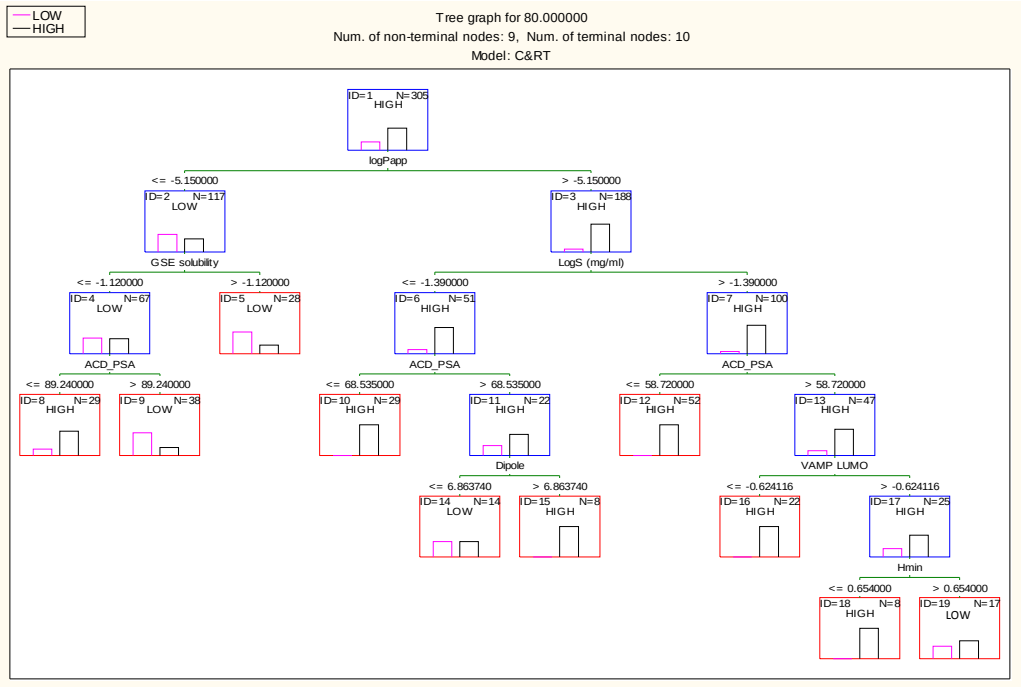
Model 3



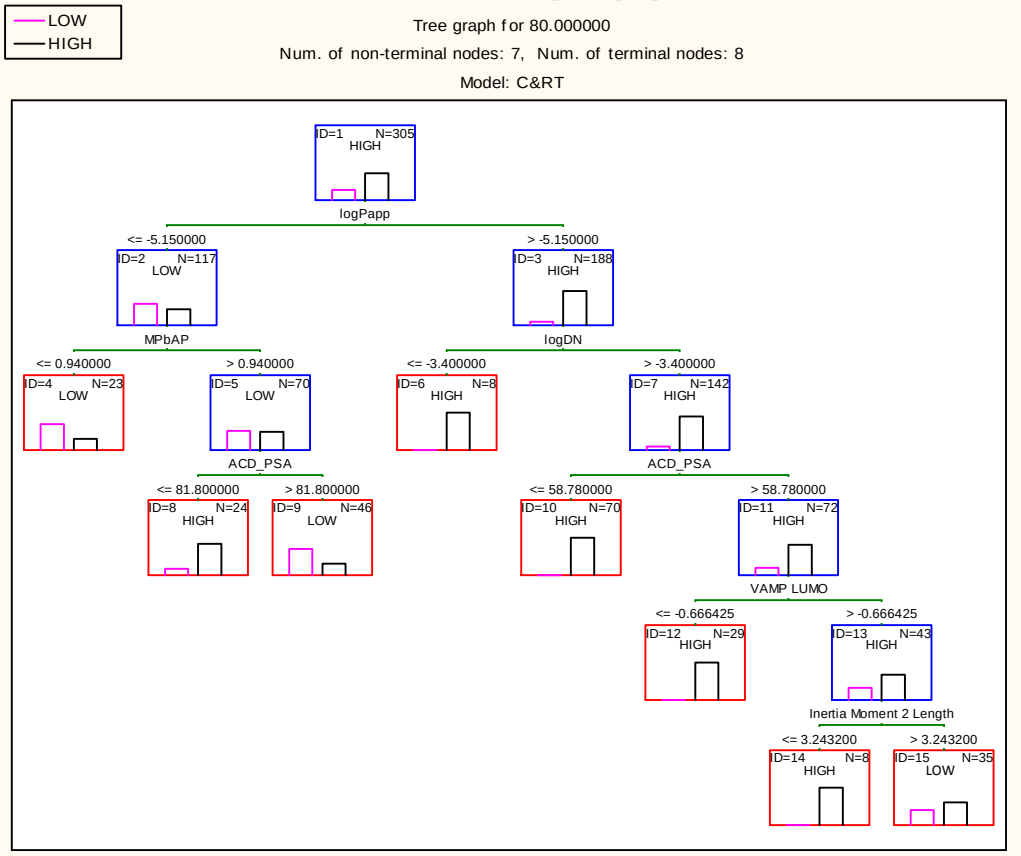
Model 4



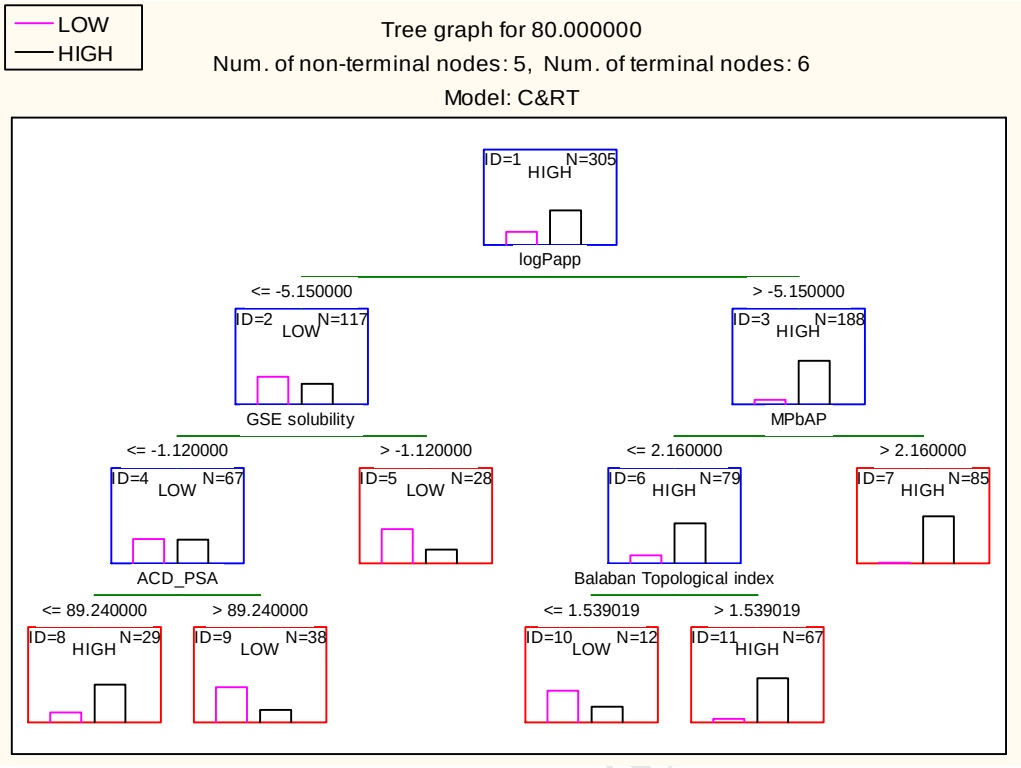
Model 5



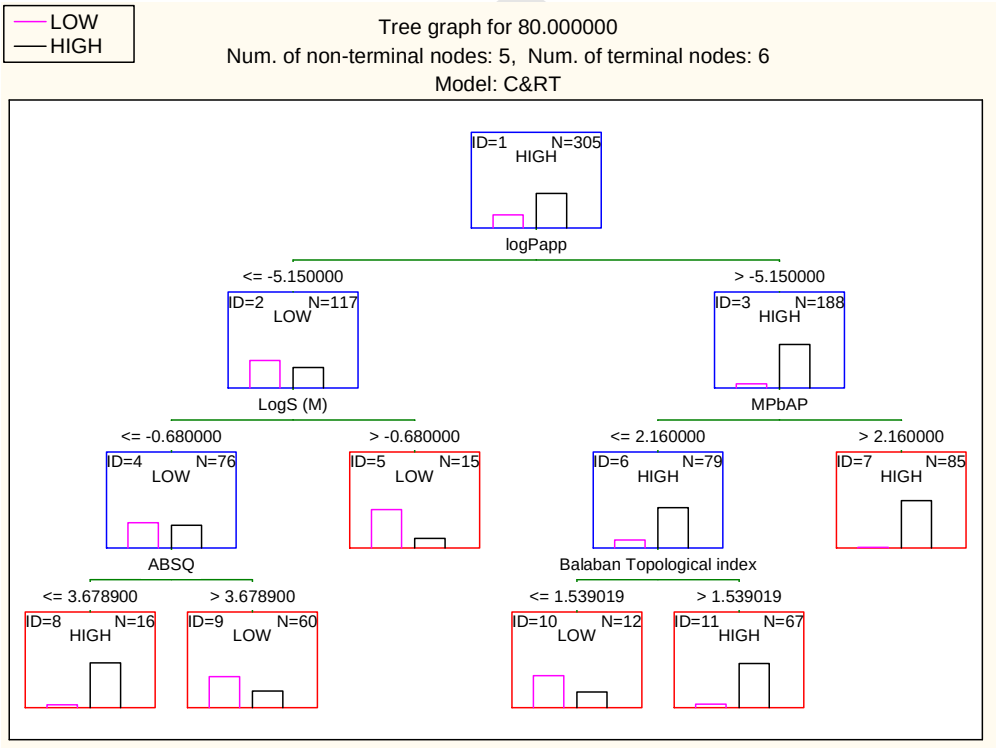
Model 6



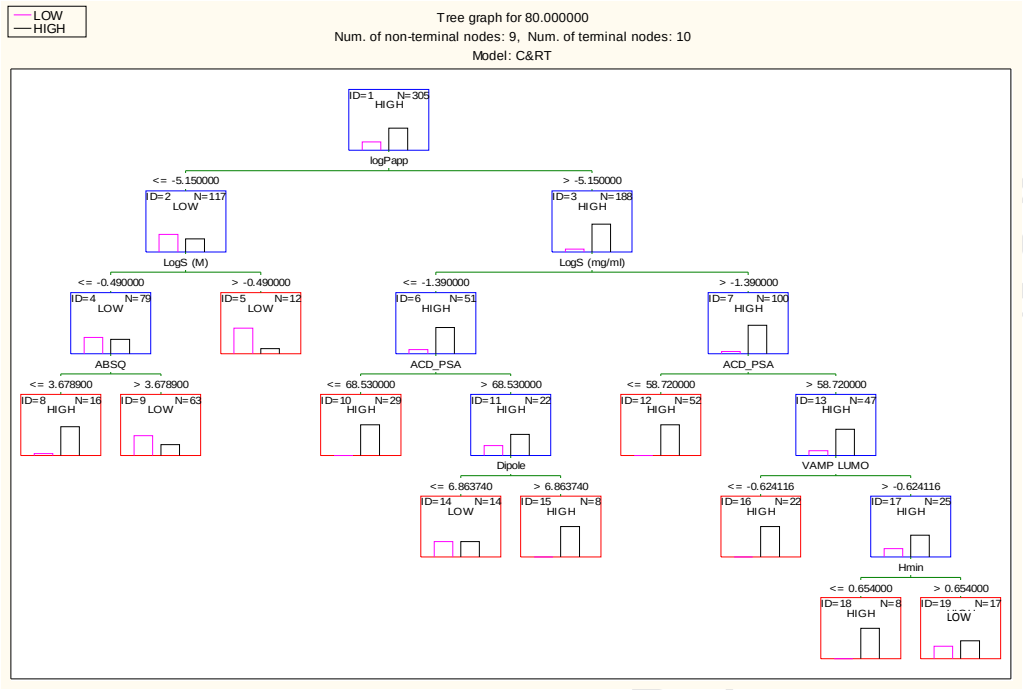
Model 7



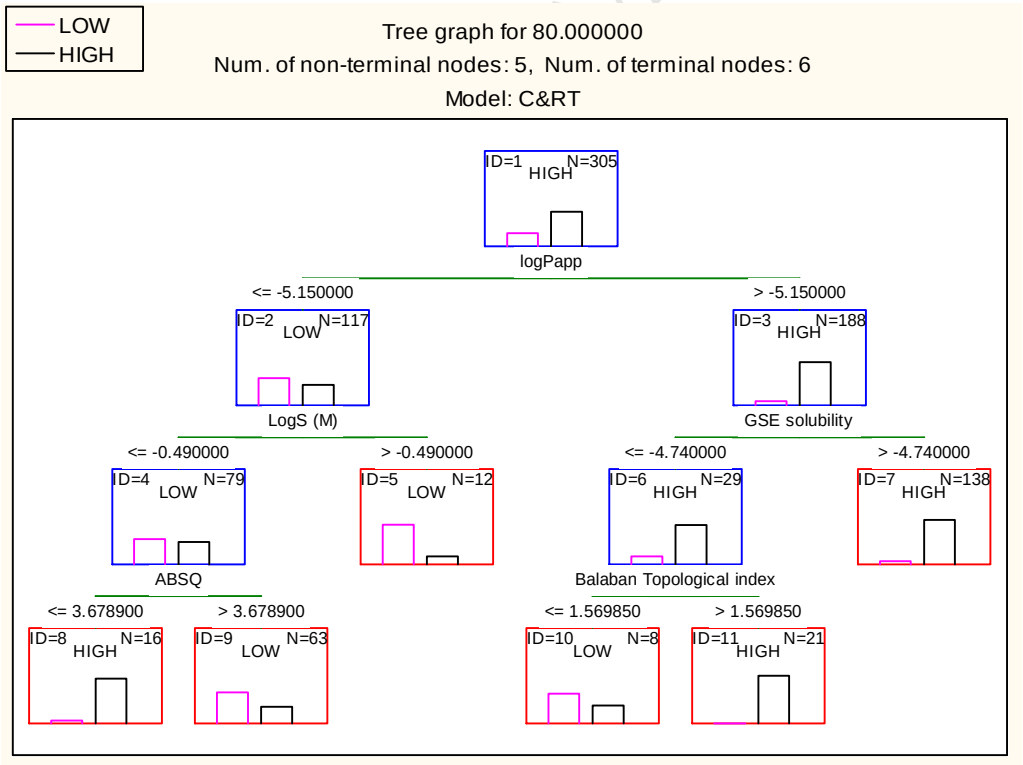
Model 8



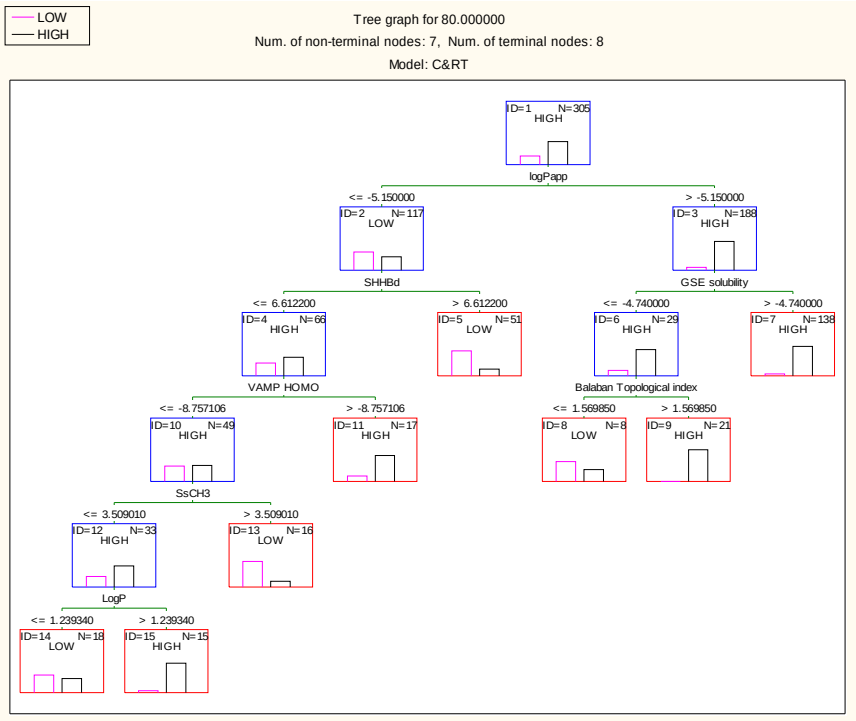
Model 9



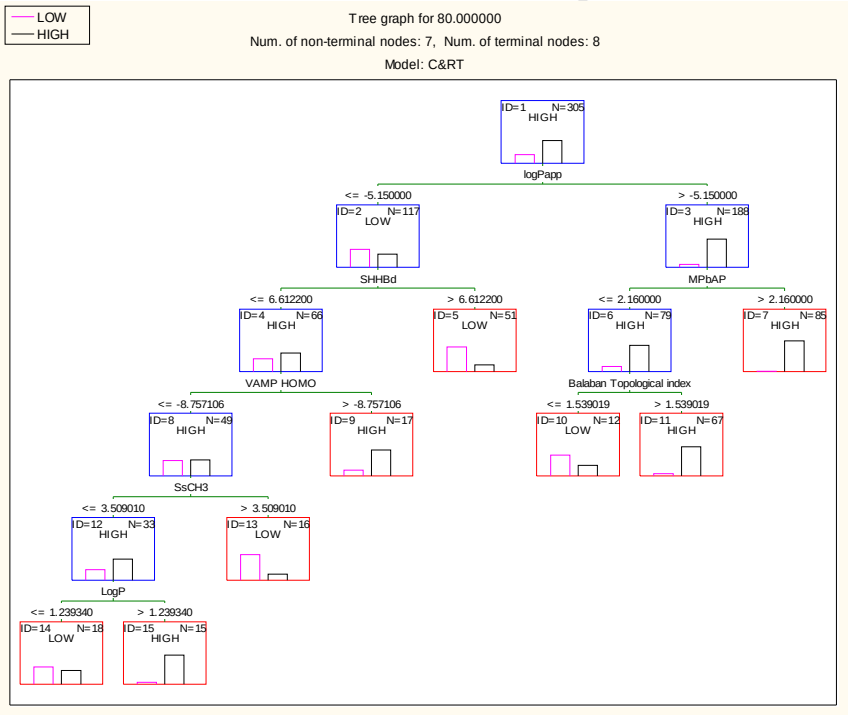
Model 10



Model 11



Model 12



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