Table 1
Classification of orally administered drugs on the WHO model list of Essential Medicines according to the BCS: *Drugs with reliable solubility and permeability data*

Drug	Solubility	Permeability	Dose (mg)	BCS class[a]	References
Abacavir antiretroviral	**High**	**Low**	**300 (sulfate)**	**III**	**[4–7]**
Acetylsalicylic acid pain relief	**High**	**Low**	**100–500**	**III*/****	**[8–18]**
Aciclovir antiviral	**High**	**Low**	**200**	**III**	**[12,19–25]**
Allopurinol gout	**High**	**Low**	**100**	**III**	**[12,16,25–31]**
Aluminium hydroxide gastro-intestinal agent	Low	Low	500	IV	[30,32–34]
Amiloride diuretic	*High*	*High*	*5 (hydrochloride)*	*I*	[12,16,30,35,36]
Ascorbic acid vitamin	**High**	**Low**	**50 (−1000)**	**III#**	**[12,16,37]**
Atenolol ß-blocker	High	Low	50; 100	III	[1,12,16,38–42]
Captopril antihypertensive	High	Low	25	III	[12,16,43,44]
Carbamazepin antiepileptic	Low	High	100; 200	II	[1,25,45,46]
Chloramphenicol antibiotic	**High**	**Low**	**250**	**III**	**[12,16,47,48]**
Chloroquine antimalarial agent	*High*	*High*	*100 (Phosphate) 150 (Sulfate)*	*I*	[12,23,25,49]
Cimetidine H2-receptor antagonist	High	Low	200	III	[12,16,38,50–56]
Sodium Cloxacillin antibiotic	High	Low	500; 1000 (Na-salz)	III	[12,16,57,58]
Codeine phosphate antitussive/analgetic	**High**	**Low**	**30**	**III**	**[12,16,59,60]**
Colchicine antigout agent	High	Low	0.5	III	[12,61–63]
Cyclophosphamide antineoplastic	*High*	*High*	*25*	*I*	[12,64–66]
Dapsone antirheumatic/leprosy	Low	High	25; 50; 100	II	[12,16,23,30,67,68]
Diazepam Benzodiazepine	*High*	*High*	*2; 5*	*I*	[12,16,25,69–72]
Digoxine cardiac glycoside	*High*	*High*	*0.625; 0.25*	*I#*	[69,73–81]
Doxycycline antibiotic	*High*	*High*	*100 (Hydrochlorid)*	*I*	[12,23,25,82]
Ergotamine Tartrate migraine	High	Low	1 (tartrate)	III*	[12,16,83–86]
Fluconazole antifungal	*High*	*High*	*50*	*I*	[16,91–95]
Furosemide diuretic	Low	Low	40	IV*	[12,38,42,56,70,96–102]
Griseofulvin antifungal	Low	High	125; 250	II	[25,79,103–105]
Hydralazine antihypertensive	High	Low	25; 50 (hydrochloride)	III*	[4,12,16,106,107]
Hydrochlorothiazide diuretic	High	Low	25	III	[1,12,16,23,30,102]
Ibuprofen pain relief	Low	High	200; 400	II	[12,25,108–110]
Indinavir antiviral	Low	Low	200; 300; 400 (Sulfat)	IV*	[4,16,30,111–113,284]
Levodopa + (Carbidopa) Parkinson's disease	*High*	*High*	*100 + 10; 250 + 25*	*I**	[12,16,30,42,114,115]
Levonorgestrel hormone	*High*	*High*	*0.15 (+0.03 Ethinylestradiol)* *0.25 (+0.05 Ethinylestradiol)* *0.75 (pack of two) + D43*	*I*	[12,16,116,117]
Levothyroxine thyroid	High	Low	0.05; 0.1 (Sodium salt)	III	[12,25,118–120]
Metformine antidiabetic	High	Low	500 (hydrochloride)	III#	[12,16,38,121–123]
Methyldopa antihypertensive	High	Low	250	III*/#	[1,12,30,124,125]
Metronidazole antibiotic	*High*	*High*	*200–500*	*I*	[12,25,126–128]
Nelfinavir antiviral	Low	Low	250 (mesilate)	IV*	[30,33,112,129,284]
Nifedipine Ca-channel blocker	Low	High	10	II*	[12,16,38,130–132]
Nitrofurantoin antibacterial	Low	High	100	II	[12,16,30,133]
Paracetamol (Acetaminophen) pain relief	**High**	**Low**	**100–500**	**III***	**[12,16,38,69,134–137]**
Penicillamine Chron. Polyarthritis	High	Low	250	III	[12,16,138–140]
Phenobarbital barbiturate	*High*	*High*	*15–100*	*I*	[12,16,23,30,141]
Phenoxy-methylpenicillin anitbiotic	*High*	*High*	*250 (Potassium salt)*	*I*	[12,25,142,143]
Phenytoin antiepileptic	Low	High	25; 50; 100	II	[12,23,25,56,144–146]
Prednisolone glucocorticoid	*High*	*High*	*5*	*I*	[16,69,147–149]
Primaquine antimalarial	*High*	*High*	*7.5; 15 (diphosphate)*	*I*	[12,150]
Promethazine antihistamine	**High**	**Low**	**10; 25 (hydrochloride)**	**III***	**[12,16,151,152]**
Propranolol ß-blocker	*High*	*High*	*20; 40 (hydrochloride)*	*I**	[1,12,38,153–155]
Propylthiouracil cystostatic	**High**	**Low**	**50**	**III**	**[12,16,30,156,157]**
Pyrazinamide tuberculotsis	*High*	*High*	*400*	*I*	[12,16,158]
Pyridostigmine Myasthenia gravis	High	Low	60 (bromide)	III	[12,159–161]
Riboflavin vitamin	*High*	*High*	*5*	*I#*	[12,16,162]
Ritonavir antiviral	Low	Low	100	IV*	[4,165,284]
Salbutamol ß-sympathomimetic	*High*	*High*	*4 (sulfate)*	*I**	[12,166–168]
Saquinavir antiviral	Low	Low	200, available as mesylate (hard gelatine capsule) or as free base (soft gelatine capsule)	IV (mesylate)/IV (free base)*	[25,30,33,112,169,284]
Stavudine antiviral	*High*	*High*	*15; 20; 30; 40*	*I*	[170–172]
Sulfamethoxazole antibiotic	Low	High	100; 400	II	[12,16,173–175]

(continued on next page)

Table 1 (*continued*)

Drug	Solubility	Permeability	Dose (mg)	BCS class[a]	References
Theophylline antiasthmatic	*High*	*High*	*100; 200; 300*	*I*	[1,12,16,176–178]
Thiamine vitamin	High	Low	50 (hydrochloride)	III[#]	[12,16,33,179]
Trimethoprim antibiotic	Low	High	100; 200	II	[12,16,173–175]
Valproic acid antiepileptic	Low	High	200; 500 (sodium salt)	II	[12,16,23,180]
Zidovudine antiviral	*High*	*High*	*300 (tablet); 100; 250 (capsule)*	*I**	[7,12,16,21,181,182]

[a] Italics denotes class I drugs according to the FDA criteria; bold text denotes class III drugs with permeabilities corresponding to at least 80% absorption.
* First pass effect; ** Degradation in the GI-Tract; [#] active transport.

the experiment was done in a buffer solution or if the pH was only adjusted with acid or base, and if the pH was checked before *and* after the experiment was conducted. Moreover, the comparison of different experiments is often difficult because of a lack of standard deviation values and statistical calculations. Some articles, however, did provide appropriate data for the BCS classification, e.g. where the intrinsic solubility of drugs (where the solubility is the lowest) was provided. If this intrinsic solubility lies between pH 1 and 7.5, the classification of the solubility of the drug can be made with the help of its pK_a and the Hendersson–Hasselbalch equation.

4.3. Permeability

Permeability data from humans is also not easy to find. As with solubility data, a database with freely available, reliable permeability data useful for BCS purposes was not found. The most common type of studies found were bioavailability studies. Since first-pass effects, degradation in the intestine and solubility-limited absorption can all influence the bioavailability, these studies can usually give at most a general indication of the permeability of the drug. The best and safest way to classify a drug as highly permeable is an absolute bioavailability study with a

Table 2
Classification of orally administered drugs on the WHO model list of Essential Medicines according to the BCS: *Drugs for which complete solubility and/or permeability data are lacking*

Drug	Solubility	Permeability	Dose (mg)	BCS class[a]	References
Acetazolamide diuretic	Low	Low	250	IV	[16,183]
Amoxicillin antibiotic	*High*	*High*	*250; 500 (anhydrous)*	*I*[#]	[1,12,16,23,30,36]
Azathioprine immunosuppressive	Low	Low	50	IV	[12,16,23,184]
Benznidazole antiprotozoal agent	*High*	*High*	*100*	*I*	[30,185]
Biperiden antimuscarinic agent	High	Low	2 (hydrochloride)	III*	[12,186]
Didanosine antiviral	High	Low	25; 50; 100; 150; 200 (buff. chew., disp tablet)	III**	[16,21,187–189]
Diethylcarbamazine anthelmentic	*High*	*High*	*50; 100 (Citrat)*	*I*	[12,165]
DL-Methionine chelating agent antidote	*High*	*High*	*250*	*I*[#]	[12,30,33]
Ergocalciferol vitamin	**High**	**Low**	**1.25**	**III**	**[12,33]**
Ergometrine postpartum haemorrhage	High	Low	0.2 (hydrogen maleate)	III	[12,190,191]
Erythromycin antibiotic	High	Low	250 (Stearat od. Ethylsuccinat)	III*/**	[12,25,33,87–90]
Ethambutol hydrochloride tuberculosis	**High**	**Low**	**100–400 (Hydrochlorid)**	**III**	**[12,16,23,33]**
Ethosuximide antiepileptic	*High*	*High*	*250*	*I*	[12,23,192,193]
Iopanoic acid contrast medium	Low	High	500	II	[12,16,30]
Isoniazid tuberculosis	*High*	*High*	*100–300*	*I**	[12,16,23,194]
Lithium carbonate antidepressant	*High*	*High*	*300*	*I*	[12,16,23,30]
Methotrexate antirheumatic/antineoplastic	High	Low	2.5 (sodium salt)	III[#]	[12,195–198]
Nalidixic acid antibacterial agent	Low	High	250; 500	II	[12,30]
Neostigmine Myasthenia gravis	High	Low	15 (bromide)	III	[12,23,160]
Nevirapine antiviral	Low	High	200	II	[30,199]
Nicotinamide vitamin	*High*	*High*	*50*	*I*	[12,16,33]
Nifurtimox antiprotozoal agent	**High**	**Low**	**30; 120; 250**	**III***	**[12,200]**
Norethisterone hormone	*High*	*High*	*1 (+0.035 Ethinylestradiol)*	*I**	[12,165]
	High	*High*	*5*	*I**	
Praziquantel antihelmentic	Low	High	150; 600	II*	[12,16,30]
Proguanil antimalarial	*High*	*High*	*100 (hydrochloride)*	*I**	[12,165]
Pyridoxine vitamin	*High*	*High*	*25 (hydrochloride)*	*I*	[12,16,201]
Reserpine antihypertensive	High	Low	0.1; 0.25	III	[12,16]
Rifampicin antituberculotic	Low	High	150; 300	II*	[12,25,68,163,164]

[a] Italics denotes class I drugs according to the FDA criteria; bold text denotes class III drugs with permeabilities corresponding to at least 80% absorption.
* First pass effect; ** Degradation in the GI-Tract; [#] active transport.

Table 3
Classification of orally administered drugs on the WHO model list of Essential Medicines according to the BCS: drugs with inconclusive data

Drug	Solubility	Permeability	Dose (mg)	BCS class[a]	References
Albendazole antiparasitic	Low	Low/High	400	II/IV*	[25,202–206]
Amitriptyline antidepressive	Low/High	High	25 (hydrochloride)	I/II*	[12,16,24,207–209]
Artemether + Lumefantrine antimalarial agents	Low	Low/High	20 + 120	II/IV*	[12,30,33,210–213]
Atropine Sulphate parasympatholytic	High	Low/High	1	I/III*	[12,16,23,32,70,214]
Chlorpheniramine antihistamine	High	Low/High	4 (Hydrogenmaleat)	I/III*	[12,16,41,151,215]
Chlorpromazine antidepressive	Low	Low/High	100 (hydrochloride)	II/IV*	[12,16,24,216,217]
Ciprofloxacin antibiotic	Low	Low/High	250 (Hydrochlorid)	II/IV*	[12,17,24,218–222]
Clofazimine antibacterial agent	Low	Low/High	50; 100	II/IV	[69,223,224]
Clomiphene hormone	High	?	50 (citrate)	I/III	[12,16]
Clomipramine antidepressive	High	Low/High	10; 25 (hydrochloride)	I/III*	[12,225,226]
Dexamethasone glucocorticoide	High	Low/High	0.5; 4	I/III*	[12,16,69,227–230]
Diloxanide antiprotozoal agent	Low	Low/High	500 (furoate)	II/IV**	[12,16,231]
Efavirenz antiviral	Low	Low/High	50; 100; 200	II/IV	[31,33,232]
Ethinylestradiol hormone	High	Low/High	0.03 (+0.15 Levonorgestrel) 0.05 (+0.25 Levonorgestrel) 0.01; 0.05;	I/III*	[12,116,233]
Folic acid	Low	Low/High	1; 5	II/IV	[12,30,234,235]
Glibenclamide antidiabetic	Low	Low/High	2.5; 5	II/IV	[12,25,38,236]
Glyceryl Trinitrate Angina pectoris	High	Low/High	0.5	I/III*	[12,237,238]
Haloperidol neuroleptic	Low	Low/High	2; 5	II/IV*	[12,16,30,70,239–243]
Isosorbid dinitrate Angina pectoris	High	Low/High	5	I/III	[16,30,244,245]
Ivermectin anthelmentic	Low	Low/High	3; 6	II/IV	[12,16,30]
Lamivudin antiviral	High	Low/High	150	I/III	[7,246–248]
Levamisole anthelmentic	High	Low/High	50; 150 (Hydrochlorid)	I/III	[202,249–251]
Lopinavir antiviral	Low	Low/High	133.3 (+33.3 Ritonavir)	II/IV*	[30,252]
Mebendazole antihelmentic	Low	Low/High	100; 500	II/IV	[25,253,254]
Mefloquine antimalarial	Low	Low/High	250 (hydrochloride)	II/IV	[16,255]
Metoclopramide prokinetic agent	High	Low/High	10 (hydrochloride)	I/III*	[12,256–260]
Morphine sulfate pain relief	High	Low/High	10	I/III*	[12,16,261–264]
Niclosamide anthelmentic	Low	Low/High	500	II/IV	[12,265]
Nystatin antifungal	Low/High	Low	100 000 IU; 500 000 IU (~5000 IU = 1 mg) - > ~20-100 mg	III/IV	[12,30,33]
Pyrantel anthelmentic	Low	Low/High	250 (embonate)	II/V	[12,165]
Pyrimethamine Toxoplasmose	Low	Low/High	25	II/IV	[12,266,267]
Quinine antimalarial	High	Low/High	300 (bisulfate or sulfate)	I/III	[12,176,268,269]
Retinol vitamin	Low	Low/High	10 000 IU (palmitate) (5.5 mg) 200 000 IU (palmitate) (110 mg)	II/IV#	[12,270,271]
Senna laxative	?	?	7.5 (sennosides)		[12]
Sodium iodide iodine deficiency	High	???	60	I/III	[12]
Spironolactone diuretic	Low	Low/High	25	II/IV*	[12,16,35,272,273]
Sulfadiazine antibacterial agent	Low	Low/High	500	II/IV	[12,23,274,275]
Sulfasalazine Colitis Ulcerosa/Morbus Crohn	Low	Low/High	500	II/IV	[12,16,276,277]
Triclabendazole anthelmentic	Low	Low/High	250	II/IV	[32,278]
Verapamil hydrochloride Ca-channel blocker	Low/High	High	40; 80 (hydrochloride)	I/II*	[1,12,16,38,70,131,221,279–282]
Warfarin Sodium anticoagulant	Low/High	High	1; 2; 5 (sodium salt)	I/II	[12,16,41,46,221,283]

*First pass effect; ** Degradation in the GI-Tract; # active transport.

bioavailability greater than 90%. In cases where the bioavailability was lower than 90%, the influence of the above-mentioned factors has to be taken into account. Where low bioavailability (< 90%) could be attributed with certainty to degradation in the GI-tract or because of a first-pass effect, these findings have been marked in the tables with asterisks. Data based on experiments where the amount of drug was measured by urinary excretion sometimes lacked i.v. comparison or determination of metabolites, both of which are necessary for a sure classification of the permeability characteristics.

Good data was found in papers using the intestinal perfusion technique in humans, as these provided direct permeability data. Data from experiments with cell culture monolayers (mostly Caco-2 cells) were often available. However, absolute values reported can vary by orders of magnitude among laboratories [3] and unless the methodology is validated according to the FDA biowaiver