

## Index

2/4/A1 cell 137

### **a**

- ABC transporter 146, 203, 228ff.
  - ABCB1, *see* MDR1 or P-glycoprotein
  - ABCB11 290
  - ABCC 244
  - ABCC1, *see* multidrug resistance-related protein (MRP) family
  - ABCC2 287
  - ABCC3 291f.
  - ABCC4 291f.
  - ABCG5 292
  - ABCG6 292
  - ABCG2, *see* BCRP
  - similarity to P-glycoprotein 498
- Abraham descriptors 386
- abraxane 601
- absorption, *see also* ADME 34, 74f., 163ff., 528
  - active 224ff.
  - animal 167ff.
  - carrier-mediated intestinal 199
  - class II drug 35f.
  - computational prediction 410ff.
  - concentration dependence 144
  - enhancement 582
  - *ex vivo* method 169
  - intestinal 187ff., 228
  - number 34
  - oral 413, 435
  - phase 582
  - model for prediction 174
  - prediction 427
  - simulation 454
  - single-pass *in situ* 170
  - solubility 145
- absorption/permeability predictor 87
- absorption rate 341

absorption rate constant 34

– effective 34

absorption scale factor (ASF) 476

absorptive intestinal transporter 245

ACAT, *see* advanced compartmental absorption and transit model

acetaminophen, *see* paracetamol

N-acetyltransferase, *see* NAT

$\alpha$ -acid glycoprotein (AGP) 119

adaptive fuzzy partitioning (AFP) 439

adefovir 293

ADME (absorption, distribution, metabolism, and excretion) 5, 73

ADME/PK

– determining parameter 169

– drug discovery 162ff.

– prediction 163

ADMET (absorption, distribution, metabolism, elimination/excretion, and toxicity) modeling 378f.

– Predictor 457

– Risk 456ff., 472f.

advanced compartmental absorption and transit model (ACAT) 456ff., 475ff.

affinity 58, 248

– PEPT1 251

albendazole 42

alfentanil 344

allometry 176

allopurinol 281

Almond descriptors 383

amiloride 194

amino acid transporter 234

$\delta$ -amino levulinic acid 227, 247

amlodipine besilate 164

amoxicillin 194ff.

amphiphilicity 86f.

anhepatic phase 343

- animal
  - absorption 167ff.
  - relevance of animal model 174
- animal bioavailability
  - prediction 441
- antipyrine 195
- antitumor agent 564f.
- APC (*adenomatous polyposis coli*) 253
- apical side 362
- apparent permeability coefficient 142
- applicability domain (AD) 63, 396f.
- aquaporin 8 238
- aqueous solubility
  - definition 11
  - drug (table) 22
  - drug discovery 10ff.
  - hit identification (HI) 12
  - lead identification 18
  - lead optimization 18
- artificial neural network (ANN) 390, 439
- associative neural network (ASNN) 59
- atenolol 193ff.
- atorvastatin 164
- atovaquone 42
- ATP binding cassette (ABC) transporter, *see also* ABC transporter
  - ATPase activity 513
  - ATPase activity assay 500ff.
  - AUC (area-under-the-curve) 3, 341
  - 3'-azido-3'-deoxythymidine (AZT) 224ff., 293
- b**
  - bacampicillin 339
  - bacteria
    - intestinal 540
  - Balaban index 379
  - bambuterol 562f.
  - base 82
  - basolateral side 362
  - Bayesian neural network (BNN) 83, 390
  - Bayesian regularized neural network (BRNN) 60
  - BCRP (breast cancer-resistance protein, ABCG2) 137, 186, 203, 236, 285ff., 365, 499, 526
    - mutation 304
  - BCUT (Burden, Cas, University of Texas) descriptor 379
  - Beer's law 106
  - bicalutamide 24
  - bile acid transporter 237
  - bile salt 38
  - biliary excretion 284
- binding 539
- bioavailability 1, 163ff., 186ff., 435
  - absolute 188f.
  - animal 167ff., 441
  - definition 1ff., 527f.
  - determining bioavailability 171
  - drug 334
  - *in silico* prediction 438ff.
  - local 598
  - nutrient 445
  - oral 1, 341, 437ff., 606
  - simulation 454, 481f.
  - systemic 598
- biopartitioning micellar chromatography (BMC) 85
- Biopharmaceutical Classification System (BCS) 34f., 190
  - application 524ff.
  - Class I drugs 35, 541
  - Class II drugs 36ff., 541
  - Class III drugs 36, 541
  - Class IV drugs 36, 541
  - permeability 190
  - redefining BCS solubility class boundary 43
  - regulatory aspect 541
  - solubility 190
- bioprecursors 566
- biorelevant media 41
- biosensor 86
- biowaiver extension potential 44
- Bjerrum plot 24
- blood-brain barrier (BBB) 80
- breast cancer-resistant protein, *see also* BCRP
  - Brij35 85
  - BSA
    - absorption 145
  - BSEP (bile salt export pump) 285ff., 308
  - bumetanide 281
  - butanilicaine 340
- c**
  - Caco-2 cell 76ff., 120, 134ff.
  - active transport 145
  - cDNA expression 363
  - gene expression profiling 238ff.
  - metabolism study 146
  - quality control 143
  - standardization 143
  - calculated log *P* (Clog *P*) 18, 83
  - calculated molecular descriptor 377ff.
  - calculated molecular properties 377ff.
  - cancer 252ff.
    - colon 253

- GIT 256
  - candidate drug 12
  - capecitabine 563
  - capillary electrophoresis 114
  - carbamazepine 194
  - carbon, labeled ( $^{14}\text{C}$ ) 169
  - $\text{l}$ -carnitine 225
  - carrier group 566
  - CART model 424
  - cassette dosing 171
  - CD147 255
  - CDH17 232, 257
  - CDX2 256f.
  - cefadroxil 246
  - cefazoline 582
  - cefixime 246
  - cell culture 134ff.
  - cell line
    - modified 360ff.
  - cell vector system 360f.
  - cell-based assay 121
  - central nervous system (CNS) 87
  - cephalexin 199, 227, 243ff., 367
  - CES 337ff.
  - chemoluminescent nitrogen detection (CLND) 17
  - chenodeoxycholic acid 227
  - Cheqsol 26, 110
  - chitosan glutamate 574
  - cholesterol 124
  - chromatographic hydrophobicity index (CHI) 83, 119
  - chromatographic method 122
  - ciliprolol 246
  - cimetidine 194
  - cisplatin 227
  - cladribine 234
  - Claritin 165
  - class II drug 36
    - Biopharmaceutics Classification System-based FDA guideline 43
    - biowaiver extension potential 44
    - dissolution 38
    - *in vitro* dissolution test 41
  - clearance (CL) 178, 295ff., 346, 437
    - biliary 300
    - total plasma 3
  - clopidogrel 564
  - colon 339, 583ff.
  - colon carcinogenesis 252f.
    - transporter 253
  - colonic water 586
  - comparative molecular field analysis (CoMFA) 250
  - comparative molecular similarity indices
    - analysis (CoMSIA) 250
  - compartmental absorption and transit model (CAT) 455
  - competition
    - prediction 514
    - competition assay 508
  - computation
    - physicochemical property measurement 88
  - computational absorption prediction 410ff.
  - consensus method 395
  - concentration dependence
    - absorption 144
  - concentrative nucleoside transporter (CNT)
    - 233
    - CNT1 243
  - constitutional descriptor 378
  - convex hull method 397
  - cosolvent mixture 112
  - creatinine 197
  - critical micelle concentration (CMC) 38, 600
  - Crohn's disease 589
  - CVODE 476
  - D-cycloserine 225ff.
  - cyclosporine 207, 224, 236, 246, 583
  - cytochrome P450 146, 189, 202ff., 336f.
    - CYP2C9 206, 336ff., 345
    - CYP3A4 146, 189ff., 202ff., 306f., 336ff., 583
    - CYP3A5 336
    - expression 363f.
    - metabolism 338, 484
  - cytotoxicity 565
- d**
- D-PAS 110
  - danazol 42
  - data
    - interpretation 126
    - presentation 126
    - set 419ff.
    - storage 126
  - degradation 539
    - luminal 539
  - delivery
    - buccal 574
    - lysosomal 604
    - modern strategy 571ff.
    - nanotechnological system 603ff.
    - oral 571ff.
    - self-assembled 600
    - tissue-selective 568
  - DEPT, *see* directed enzyme-prodrug therapy

- descriptors 58, 378ff.
  - 3D 381
  - absorption 410f.
  - Almond 383
  - constitutional 378
  - fragment- and functional group-based 378
  - hydrogen bonding 80
  - Jurs 382
  - quantitative prediction of oral absorption 419
  - qualitative prediction of oral absorption 420
  - topological 379
  - WHIM 381f.
- desipramine 225
- detection methodology 14ff.
  - chemoluminescent nitrogen detection (CLND) 17
  - turbidimetric method 14
  - UV absorption method 15
- 1,2-dichloroethane (DCE)/water system 83
- diffusion
  - paracellular passive 193
  - passive 80, 142
  - transcellular passive 196
- digoxin 226ff., 246
- dipyridamole 39
- directed enzyme-prodrug therapy (DEPT) 567
- dissociation constant 110
  - cosolvent mixture 112
  - measuring 111ff.
  - separation 113
- dissolution 76, 528ff.
  - gastrointestinal 38ff.
  - *in vitro* test 41
  - number 34f.
  - testing requirement 552
  - volume 41
- distance-based method 397
- distribution, *see also* ADME 76
  - *in silico* estimation 481
  - volume 76, 437
- distribution coefficient 81
- DMSO 13f., 105, 117f.
  - aqueous solubility 10ff.
  - solubility assay 18
- DNA 598ff.
- donor 362
- well 123f.
- L-dopa 194ff.
- dose 550
  - prediction in man 176f.
- dose number 34f.
- dosing 585
  - time 585
- doxorubicin 236, 508
- dried-down solution method 20
- drug 2
  - active absorption 224ff.
  - active uptake (table) 479
  - bioavailability 334ff., 598ff.
  - candidates 12, 544
  - class II 36ff.
  - degradation 540
  - delivery 599ff.
  - development 481f., 543
  - discovery 102
  - efflux (table) 479
  - high-solubility 533ff.
  - intestinal transport and absorption 134ff.
  - low-solubility 546
  - metabolism 208
  - metabolism and pharmacokinetics (DMPK) 9, 73ff.
  - oral absorption 140
  - particle size 40
  - physicochemical property 73ff.
  - rule-based ranking (table) 459ff.
  - transport 208
  - transport assay 362
- drug-drug-interaction 309
- transporter-mediated 305
- drug-likeness 87
- drug-loading capacity 601
- druggability 34, 456, 528
  - physicochemical approach 73ff.
- DSSTox (distributed structure-searchable toxicity) database network 473
- e**
- effective absorption rate constant 34
- effective intestinal permeability 535
- efflux
  - mechanistic correction 478
  - protein 526
  - sinusoidal 290
  - transporter 236, 365
- electromotive force (E, emf) 111
- electrotopological state index 379
- enalapril 194ff.
- enalaprilate 194
- endocytosis 604
- endosome 604
- ensemble method 395
- enteric coating 539
- enterocyte 191ff.
  - compartment 480

- Environmental Protection Agency (EPA) 473  
 epithelial-mesenchymal transition (EMT) 252ff.  
 equilibrative nucleoside transporter (ENT)  
   – ENT2 243  
   erythromycin 281  
   ESI mass spectrometry detection 122  
   esophagus 573f.  
   etoposide 226ff.  
   *ex vivo* method  
   – absorption 169  
   excretion, *see* ADME  
   extended release (ER) 538ff.
- f**  
 familial adenomatous polyposis (FAP) 253  
 FaSSIF (fasting-state simulated artificial intestinal fluid) 78  
 FDA guideline  
   – Biopharmaceutics Classification System-based 43  
 fed-state simulating intestinal fluid (FeSSIF)  
   42  
 fenazon 194  
 fexofenadine 194, 207  
 fingerprint 378  
 first-pass effect 572  
 flow cytometry 109  
 flow injection analysis (FIA) 109  
 fludarabine 225ff.  
 5-fluorouracil 281, 563  
 fluoxetine 164  
 fluticasone propionate 56  
 fluvastatin 194ff., 206f.  
 food-drug interaction 549  
 formulation  
   – nanotechnological 601  
 formulation principle 545  
   – solid 545  
 fraction absorbed 417  
 fractional factorial design (FFD) 398  
 fragment- and functional group-based descriptor 378  
 free energy of binding 511  
 furosemide 194ff.
- g**  
 gas chromatography 113  
 gastric emptying 579ff.  
 gastric inhomogeneity 576  
 GastroPlus program 55  
 gastrointestinal (GI)  
   – characteristics 530  
   – dissolution 38ff.  
   – pH 39  
   – simulation 454f.  
   – transit 39  
 gastrointestinal tract (GIT) 166, 185ff., 530f., 572  
   – lower 583ff.  
   – mid 576ff.  
   – transporter 223ff.  
   – upper 573ff.  
 Gaussian process (GP) 60  
 gemcitabine 225  
 gene expression profiling 238  
 general solvation equation 412  
 genetic algorithms (GA) 394  
 genetic programming 394f., 426  
   – algorithm 440  
 genetic rule extraction (G-REX) 426  
 genotype 242  
 geometric method 397  
 glucose 195f., 225  
 glucose transporter 246  
   – GLUT2 232  
   – GLUT5 234  
   – sodium coupled (SGLT1) 246  
 glutathione S-transferase (GST) 208  
 GRID probe 383  
 grid-independent descriptor (GRIND) 510  
 griseofulvin 43  
 gut wall 335  
   – first-pass metabolism 347  
   – metabolism 334ff.
- h**  
 half-life 438  
 half-transporter 499  
 halofantrine 43  
 hCE-1 (human carboxylesterase 1) 147  
 HDM (hexadecane membrane) 85  
 Henderson-Hasselbalch relationship 82, 110  
 hepatic efflux process 298  
 hepatic intrinsic clearance 444  
 hepatic portal vein cannulation 173  
 hepatic transport 278ff.  
 hepatic uptake 278f., 294f.  
 hepatobiliary transport 299  
 hereditary nonpolyposis colorectal cancer (HNPPCC) 253  
 hERG (human ether-a-go-go related gene) 474  
 heuristic molecular lipophilicity potential (HMLP) 385  
 high-throughput log  $D_{7,4}$  measurement 117

- high-throughput log  $D_{\text{pH}}$  measurement 118  
 high-throughput measurement 106ff.  
 – physicochemical property 106ff.  
 high-throughput screening (HTS) 102  
 high-throughput solubility (HTSol) assay 14  
 – kinetic 14  
 – thermodynamic 14  
 hit identification (HI) 12  
 hit-to-lead stage 105, 428  
 hologram QSAR (HQSAR) 440  
 hPEPT1 199ff.  
 HPT1 232f., 256f.  
 HT29 cell 139  
 human immunodeficiency virus (HIV)  
 inhibitor 246  
 human serum albumin (HSA) 119  
 HYBOT descriptor 386  
 hybrid potentiometric/UV spectrometric  
 technique 112  
 hydrochlorothiazide 194  
 hydrogen bond  
 hydrogen bond acceptor (HBA) 413, 435, 511  
 hydrogen bond donor (HBD) 413, 435,  
 511  
 hydrogen bonding 80  
 hydrophobic surface property 382  
 hydrophobicity 81
- i**
- ibuprofen 39  
 IEC-18 cell 140  
 immediate release (IR) 36  
 immobilized artificial membrane (IAM)  
 83ff., 119  
 immobilized liposome chromatography  
 (ILC) 85  
*in vitro* – *in vivo* correlation (IVIVC) 41, 191,  
 536, 547ff.  
*in vivo* human permeability database 187  
*in vivo* method  
 – determining bioavailability 171  
*in-house* model 63  
 inflammation 252  
 inflammatory bowel disease (IBD) 259  
 influenza 561f.  
 inhalation 173  
 inhomogeneity  
 – gastric 576  
 intestinal absorption 188f.  
 – carrier mediated 199  
 intestinal barrier permeation 512  
 intestinal drug transport and absorption  
 134ff.  
 intestinal metabolism 342ff.
- intestinal mucosa  
 – physiology 334  
 – profiling 238  
 intestinal perfusion technique 187ff.  
 – *in vitro* 190  
 intestinal permeability 134  
 – effective 535  
 intestinal stem cells 258  
 intestinal transporters 242  
 – absorptive 245  
 intestine 238f., 339, 576  
 – active transport 228  
 – disease 251  
 – transporter 251  
 ion exchange chromatography 113  
 ionization 78f., 413  
 ionized form 79  
 isocarboxazid 340  
 isosbestic point 107
- j**
- jejunal transport 202f.  
 Jurs descriptors 382
- k**
- k*-nearest neighbor (KNN) 59  
 – modeling 392  
 ketoconazole 39ff., 205ff.  
 ketoprofen 39ff., 194  
 Kier-Hall indices 379
- l**
- lansoprazole 164  
 large neutral amino acid (LNAA) 201  
 LAT1 244  
 lazar (lazy structure-activity relationship)  
 method 398  
 lead generation phase 428  
 lead identification (LI) 12ff.  
 – thermodynamic solubility 26f.  
 lead optimization (LO) 12ff., 428f.  
 – thermodynamic solubility 26f.  
 Leadscope fingerprint 378  
 leave-multiple-out cross validation  
 (LMO-CV) 399  
 leave-on-one-out cross validation (LOO-CV)  
 399  
*L*-leucine 197  
 linear discriminant analysis (LDA) 392, 510  
 linear method 388  
 linear solvation energy relationship (LSER)  
 58  
 lipid bilayer 122  
 lipid-DNA nanoparticulate 607

- Lipinski's rule-of-5, *see* rule-of-5  
 Lipitor 164  
 lipolysis model  
   – dynamic 42  
 lipophilicity 74ff., 115ff., 413  
   – effective 82  
   – intrinsic 81  
   – measuring 116  
 liposome 600ff.  
   – partitioning 86  
 liquid chromatography/mass spectrometry  
   (LC/MS) 109, 122  
 lisinopril 194ff.  
 liver 189f., 335  
   – basolateral membrane 293  
 LLC-PK<sub>1</sub> cell 363  
 local drug bioavailability  
   – improved 606  
 local model 65  
 Loc-I-Gut® technique 187ff., 537f.  
 $\log D$  81  
   – calculated 83  
 $\log P$  ( $\log_{10}$  of water/octanol partition coefficient) 81, 385  
   – calculated 18, 83  
   – versus  $\log D_{\text{pH}}$  247  
 loratadine 165  
 losartan 194ff.  
 Losec 164  
 lung 174  
 lysophospholipid 603
- m**
- macromolar prodrugs 566  
 Madin-Darby canine kidney (MDCK) cell 120, 136f.  
   – cDNA expression 363  
 Mahalanobis distance 63  
 MATE (multidrug and toxic compound extrusion) 285ff.  
 maximal absorbable dose (MAD) 77  
   – calculation 55  
 maximal recommended therapeutic dose (MRTD) 473f.  
 MDR1 (multidrug resistance transporter), *see* P-glycoprotein  
 medication  
   – orally administered 571ff.  
 melphalan 227, 244  
 melting point (MP) 58  
 membrane  
   – artificial 83ff.  
   – bile canalicular 308  
   – composition 123  
   – diffusion 196  
   – HDM 85  
   – permeability 84, 412  
   – sinusoidal 305  
   – transporter 242  
 membrane barrier permeation 512  
 membrane potential change 249  
 metabolic enzymes 363  
 metabolism, *see also* ADME 202, 442  
   – drug 108  
   – gut wall first-pass 347  
   – hepatic first-pass 342  
   – *in silico* estimation 484  
   – intestinal 342ff.  
   – presystemic 188f.  
   – simulation 454  
   – study 146  
 methotrexate 281  
 $\alpha$ -methyldopa 194ff.  
 metoprolol 194, 482  
 micellar electrokinetic chromatography (MEKC) 85  
 microemulsion electronic chromatography (MEEKC) 119  
 microscopic analysis 22  
 midazolam 482  
 model 63ff.  
   – 3D-QSAR pharmacophore 509f.  
   – applicability domain 63  
   – development 419  
   – predictive *in silico* 508  
   – validation 399  
 modeling 484f.  
   – QSAR 88  
 modular binding approach 511  
 molecular descriptor  
   – 2D-based 377  
   – calculated 377ff.  
 molecular interaction field (MIF) 383  
 molecular lipophilicity potential (MLP) 385  
 molecular property  
   – calculated 377ff.  
 molecular lipophilicity potential (MLP) descriptor 83  
 molecular size 79  
 monocarboxylate transporter (MCT) 235, 526  
 monosaccharide transporter 234  
 montelukast 10  
 mRNA expression profiling 240  
 MRP, *see* multidrug resistance-related protein family  
 mucosa 334ff.  
   – buccal 574

- intestinal 334ff.
- multidrug resistance transporter, *see* MDR1
- multidrug resistance-related protein (MRP)
  - family 136, 197, 526
  - MRP1 (ABCC1) 186, 236, 292f., 365, 499
  - MRP2 137ff., 236, 286ff., 304ff., 361ff.
  - MRP3 186, 236, 291
  - MRP4 291f.
  - MRP5 292f.
  - MRP6 292f.
- multiple indicator dilution (MID) method 294
- multiple linear regression (MLR) 59, 388, 439
- multivariate statistical analysis 387ff.
  
- n**
- nanocarrier
  - single-molecule-based 601
- nanocrystal 599
- nanoparticulate
  - biological stability 602
  - processed 601f.
  - self-assembling 600
- nanosystem 606
- improved oral drug bioavailability 606
- nanotechnological formulation
  - pharmaceutical property 601
- nanotechnology 597ff.
  - delivery 603ff.
- naproxen 194
- NAT (N-acetyltransferase) 340
- nephelometer 109
- nephelometric detection 14
- neuraminidase inhibitors 561f.
- neutral forms 79
- neutral species 115
- new chemical entity (NCE) 245
- nifedipine 25, 364, 574
- non-polar surface area (NPSA) 413
- non-steroidal anti-inflammatory drugs (NSAID) 43
- nonsink analysis 142
- Norvasc 164
- Noyes-Whitney model 38, 529
  - Nernst-Brunner and Levich modification 38
- NTCP ( $\text{Na}^+$  taurocholate cotransporting polypeptide) 278ff., 308
- nucleoside transporter
  - concentrative (CNT) 233
  - equilibrative (ENT) 233
- nutrient
  - bioavailability 445
  - nutrient absorption carrier 551
  
- o**
- OAT, *see* organic anion transporter
- OATP, *see* organic anion transporting peptide
- octanol/water distribution coefficient 83
- OCT, *see* organic cation transporter
- Ogast/OgastORO 164
- Oie-Tozer equation 76
- olanzapine 165
- omeprazole 164, 539
- onion design (OD) 398
- oral absorption 436ff.
  - computational model 413
  - definition 436
  - improved 606
  - qualitative prediction 420ff.
  - quantitative prediction 413ff.
- oral bioavailability, *see* bioavailability
- ordinary differential equation (ODE) 474
- organic anion transporter (OAT) 281ff.
  - (OATP) 235, 278ff.
  - OATP1A2 281, 367
  - OATP1B1 137, 278ff., 301ff., 365
- organic cation transporter (OCT) 201f., 235, 284
- OCNT1 201f., 235
- OCNT2 201f., 235
- oseltamivir 562
- OST $\alpha/\beta$  292
  
- p**
- p53 253
- P-glycoprotein (P-gp, ABCB1, MDR1) 81, 136ff., 186, 196ff., 203, 254, 286ff., 361ff.
- ATPase activity assay 500f.
- function 500
- mutation 301
- similarity to other ABC transporter 498f.
- structure-activity relationship 498ff.
- paclitaxel 226ff., 246, 281
- paracellular passive diffusion 193
- paracetamol 578
- parallel artificial membrane permeation/permeability assay (PAMPA) 75, 84, 120ff.
- calculation of permeability 124
- gastrointestinal 123
- *in silico* 85
- paroxetine 165
- partial least squares (PLS) 61, 389
- partition coefficients 176

- partitioning method 393  
 PASS 87  
 passive flux 507  
 PAT1 234  
 peptide transporter 232f.  
   – PEPT1 147, 199, 224ff., 247ff., 259f., 367,  
     526, 551  
   – PEPT2 367  
   – prediction of affinity 251  
 percentage absorbed 480  
 perfusion method 170  
 permeability 34, 74f., 84ff., 119ff., 442  
   – apical-to-basolateral 122  
   – apparent 125  
   – apparent permeability coefficient 142  
   – basolateral-to-apical 122  
   – calculation from PAMPA data 124  
   – effective 125  
   – *in vitro* model 84  
   – *in vivo* 537  
   – *in vivo* study 185ff.  
   – intestinal 134  
   – jejunal 206  
   – membrane 84  
   – pathophysiological effect 589  
   – surface property 126  
 pH  
   – absorption 144  
   – gut 589  
   – partition hypothesis 455  
 pharmaceutical objectives 560  
 pharmacodynamic objectives 564  
 pharmacodynamic (PD) processes 3  
 pharmacodynamics 525  
 pharmacokinetic model  
   – physiological 177  
 pharmacokinetic objective 561  
 pharmacokinetic (PK) processes 2f.  
 pharmacokinetics 74, 437, 525  
   – physiologically based 176  
 pharmacophore fingerprint 384  
 pharmacophore models  
   – 3D-QSAR 509f.  
 phloridzin 246  
 phosphatidylcholine 124  
 phosphatidylethanolamine 124  
 phosphatidylinositol 124  
 phosphatidylserine 124  
 physicochemical factor 34  
 physicochemical parameter 531  
 physicochemical property  
   – high-throughput measurement 106ff.  
 physicochemical property measurement  
   – computation 88  
 physicochemical screening 102ff.  
   – high-throughput profiling 104  
 physiological modeling 443  
 physiological parameter 531  
 physiologically-based pharmacokinetic  
   (PBPK) 78, 310  
   – *in silico* estimation of distribution 481  
   – modeling 86, 444  
 plasma concentration 178  
 plasma protein  
   – binding 76  
 polar surface area (PSA) 58, 80, 386, 413  
 polarity 413  
 polarized light microscopy (PLM) 22  
 positron emission tomography (PET) 310  
 potassium channels 474  
 potentiometry 24  
 powder X-ray diffraction (PXRD) 22  
 pravastatin 225ff., 283  
 precipitate detection 109  
 prediction  
   – animal bioavailability 441  
   – hepatic efflux process 298  
   – *in silico* prediction of human  
     bioavailability 434ff.  
 prodrug 559ff.  
   – strategy 560  
   – type 565f.  
 progesterone 43  
 property-based descriptor 385  
 propranolol 194, 482  
 Prozac 164  
 pSol 24  
 public model 63
- q**
- quality by design (QbD) 552  
 quantitative structure-activity relationships  
   (QSAR) 66, 400  
   – 3D-QSAR pharmacophore models 509f.  
   – combinatorial 88  
   – binding of drugs to transporter 249  
   – descriptors 66  
   – *in silico* QSAR model of oral  
     bioavailability 438  
   – modeling 88  
 quantitative structure-property relationships  
   (QSPR) 56
- r**
- radiolabel 169  
 Raman microscopy 22  
 ramipril 339  
 range-based method 397

- ranitidine 194, 281  
 ranking  
   – rule-based (table) 459ff.  
 receiver 362  
   – well 123f.  
 receiver-operating characteristic (ROC)  
   curve 425  
 relative activity factor (RAF) 295  
 reversed-phase high-performance liquid  
   chromatography (RP-HPLC) 81, 113ff.  
 RNA  
   – siRNA 598  
 root mean square error of predictions  
   (RMSE) 59  
 rotating-disk method 529  
 rule extraction  
   – genetic programming-based 426  
 rule-based method 393f.  
 rule-based ranking (table) 459ff.  
 rule-of-5 87, 435, 512
- s**
- saquinavir 482  
 semisimultaneous dosing 172  
 Seroxat 165  
 sertraline 165  
 SGLT1 246  
 shake-flask method 22, 104  
   – log  $D_{7,4}$  117  
 shape 79, 413  
 simulated gastric fluid (SGF) 42  
 simulation 454ff., 484f.  
   – mechanistic 474  
 simvastatin 164, 339  
 single-nucleotide polymorphism  
   (SNP) 242  
 single-pass *in situ* absorption 170  
 single-photon emission computed tomography  
   (SPECT) 310  
 sink condition 125, 191, 534  
   – binding-maintained 125  
   – ionization-maintained 125  
   – physically-maintained 125  
 siRNA 598  
 size descriptor 79  
   – calculated 79  
 SLC, *see* solute carrier family  
 small intestinal transit pattern 581  
 sodium decanoate 582  
 soft drug 560  
 soft independent modelling of class analogy  
   (SIMCA) 440  
 software for aqueous solubility 61  
 solid  
   – solubility 21  
   – supernatant concentration method 109  
   – state characterization 22  
 solubility 54, 76f., 104ff., 412, 528  
   – absorption 145  
   – aqueous, *see* aqueous solubility  
   – calculated 78  
   – DMSO-based 18  
   – dried-down solution method 20  
   – high-throughput (HTSol) 14  
   – *in silico* prediction 54ff.  
   – *in vivo* 550  
   – intrinsic 24  
   – kinetic 104  
   – measuring 104ff.  
   – method 104ff.  
   – modeling 56ff.  
   – pH range 107  
   – potentiometry 24  
   – rate (SR) 531  
   – solid 21f.  
   – thermodynamic 22ff., 104  
 solute carrier (SLC) family 228ff., 254  
   – SLC2A2 232  
   – SLC10A1 279  
   – SLC15A1 224ff., 243  
   – SLC19 254  
   – SLC22 281ff.  
   – SLC28A1 232  
   – SLC29A1 232  
   – SLC31A1 254  
   – SLC38A 254  
   – SLC47A1 290  
   – SLC5A1 232  
   – SLC5A8 255  
   – SLCO 278f.  
   – SLCO1B1, *see also* OATP1B1 301ff.  
   – systematic nomenclature 278  
 static method 169  
 statistical method 387ff.  
 stem cells  
   – intestinal 258  
 stomach 339, 572ff.  
 structure-activity relationships (SAR) 400,  
   509  
   – P-glycoprotein 498  
 substrate-transporter affinity 504  
 substrate-transporter interactions  
   503f.  
 sucralfate 575  
 sulfotransferase (SULT) 337ff.  
 supernatant concentration 106ff.

- support vector machine (SVM) 59, 390f., 425
- surface plasmon resonance (SPR)  
technology 86
- t**
- tacrolimus 226ff.
- talinolol 226ff.
- target factor analysis (TFA) 112
- targeting  
– intracellular 604
- tenofovir 293
- terbutaline 195f., 563
- test set selection 398
- tetracycline 281
- theophylline 281
- thermodynamic solubility 22ff.  
– application in LI and LO 26f.
- thin-layer chromatography (TLC) system 81
- tight junction 199, 607
- tirapazamine 564f.
- tissue barrier 603
- TMF (transport, metabolism, and blood flow) 346
- 4-toluenesulfonylureido-carnosine 227, 248
- topological descriptors 379ff.
- TOPS-MODE method 423
- total plasma clearance 3
- toxicity, *see also* ADMET 567  
– database 473
- toxicology 598
- training set 398
- transcellular passive diffusion 196
- transepithelial electrical resistance (TEER) 477
- Transil 86
- transit 581ff.  
– colonic 584f.  
– pathophysiological effect 587
- translocation 248
- transport 186ff., 208  
– active 301  
– apparent 513  
– assay 506  
– hepatobiliary 294  
– intrinsic 513  
– jejunal 202f.  
– rate 504
- transport experiment 141  
– active 145, 478
- transporters  
– ABC 146, 203, 228ff.
- amino acid 234
- ATP-complex 502
- bile acid 237
- colon cancer 253
- drug absorption targeting 245
- efflux 365f.
- expression 365
- gastrointestinal tract (GIT) 223ff.
- intestinal 242
- large neutral amino acid (LNAA) 201
- monocarboxylate (MCT) 235
- monosaccharide 234
- nucleoside 233
- organic anion 235
- organic cation 235
- overall hepatic uptake 295
- peptide 232f.
- tumor suppressor 255
- uptake 367
- tritium ( $^3\text{H}$ ) 169
- troglitazone 42
- tumor stroma interaction 255
- tumor suppressor gene 255
- turbidimetric method 14
- turbidity measurement 109
- u**
- UDP-glucuronosyltransferase (UGT) 337ff.  
– UGT1A1 208, 337
- unstirred water layer (UWL) 85, 121ff., 196
- uptake 309  
– active 479
- transporter 367
- urea 197
- Ussing diffusion chamber 345
- UV absorption method 15
- UV spectrometric technique 112
- v**
- valaciclovir (valacyclovir) 224, 246, 367
- valganciclovir 246
- valproic acid 235
- verapamil 194ff., 225
- vigabatrin 225ff.
- villus 335
- visualization  
– on-the-fly 107
- VolSurf descriptors 383
- volume  
– distribution 437
- model for prediction 175

**w**

WHIM (weighted holistic invariant molecular descriptors) 381f.  
Wiener index 379  
World Drug Indices (WDI) 87

**y**

Yalkowsky equation 58  
Yasuda-Shedlovsky technique 113

**z**

Zagreb indices 379  
zanamivir 561f.  
zidovudine 281, 293  
Zocor 164  
Zoloft 165  
Zyprexa 165