

INDEX

- ABC complex, 296
ABCG2, 382, 395
ABCP, 382, 395
Absorption, 74
Accumulation, 81
Acute dosing, 80
Acyclovir, 129
ADEPT, 135, 363, 373, 203, 231
Adherens junctions, 18, 19, 25
ADME, 74, 78
Aerosol, 2, 3, 4, 5, 7, 9, 11, 13, 22, 23, 25, 26, 30
Aldophosphamide, 213
Alveolar epithelium, 111–114
Amino-dendrimer, 280
Aminotransferase, 79, 80
Amphipathicity, 284
Amphipathic helices, 285
Amorphous, 62, 63, 65
Ampicillin, 128, 143
ANDA, 439, 440, 437
Anthracyclines, 383, 385, 390, 391, 395
Antibody-mediated translocation, 363, 374
Antibody (recombinant), 363–376, 371, 372
Anticholinergic, 11
Antigen, 282
Antioxidant, 9, 13
Antp, 284
Aromatic nitro-containing anticancer prodrugs, 206
AQ4N, 134
Asthma, 3, 9, 11, 12, 13, 27
Azo prodrugs, 147
Azoreductase, 132
BAA, 10
Bacampicillin, 128, 140
BBMEC, 25
BCRP, 381, 382, 385, 394–396
Balsalazide, 132, 147
Bexxar, 368
Bile salts, 1, 7, 9
Biliary excretion, 382, 388, 389, 393, 394, 396–398
Bioavailability, 74, 75, 76, 81, 281
Bioluminescence, 76
Biophase, 76
Bioreductive activation, 133
Blood-brain barrier, 16, 23, 109–111, 284, 259
Blood-retinal barrier, 115

- Blood stream, 75, 76, 78
 Brain, 259
 Bronchodilation, 10
 Brownian motion, 292
 BSEP, 381, 382, 397, 398
- Caco-2, 24
 Caco-2 cells, 107–108, 113
 Calcium chelators, 7
 Campath, 364
 Camptothecins, 226
 Cancer, 250
 Candesartan, 140
 Candesartan cilexetil, 140
 Carbapenems, 141
 Carboxypeptidase G2 (CPG2), 232, 238
 Cascade prodrugs, 139, 140, 149, 157
 CB1954, 134, 135
 Calcitonin, 10
 Catenin, 19
 Cathepsin B, 213, 220
 Cationic lipids, 412, 424
 Cefuroxime axetil, 140
 Cell adhesion, 19
 Cellular uptake, 280
 Chelating agent, 9
 Chemical modifications, 10, 13
 Chemical tractability, 6
 Chemotherapy, 250, 253
 Chitosan, 7
 Chloramphenicol, 131
 Chloramphenicol palmitate, 131
 Chloramphenicol sodium succinate, 131, 132
 (2-Chloroethyl)-(2-mesyloxygen)-
 aminobenzoyl-L-glutamic acid
 (CMDA), 233
 Chromatin, 281
 Ciliary neurotrophic factor, 280
 Cognex, 440
 Collagenases, 213
 Combinatorial chemistry, 74
 Combretastatin A-4, 221
 Complex, 307, 309–313
 Complexing agent, 13
 Conformational stabilizer, 13
 Controlled release, 58, 66, 67, 68
 Coralyne, 150
 Corneal epithelium, 114–115
 Corticosteroids, 12
 Claudin, 19
 Cleavable linkers, 173
 Clinical trials, 2, 3, 6
- Cromones, 12
 Cryoprotectant, 13
 Crystalline, 61, 62, 63
 CpG motif, 308, 309
 Cyclodextrin, 61, 64
 Cyclophosphamide, 230, 238
 Cyclosporine, 385–387, 389–391, 395
 CYP, 21, 22, 23
 CYP450 enzymes, 107–109
 Cystic fibrosis, 13, 20, 28
 Cytochrome P450, 229, 231
 Cytoskeleton, 283
- Degradation, 308, 309, 313, 2, 9, 11, 21, 30,
 32
 Delivery, 281, 282, 287–291, 295, 296
 Delivery vector, 281
 Desglymidodrine, 145
 Desmocollin, 20
 Desmoglein, 20
 Desmosomes, 18, 20
 Developability criteria, 5–10
 Development, 73, 74, 80
 Digoxin, 385, 387–390, 397
 Degradation pathways, 62–64
 Dinitrobenzamide mustards, 135
 Distribution, 307–310, 313, 74, 76
 Dissolution, 59, 60, 61, 62, 64, 65, 67
 Disulfide bond, 288
 Diphtheria toxin, 283
 DMPK, 7, 9
 DNA, 306–314, 280, 282, 287, 291, 293
 Dose regimen, 74
 Doxorubicin, 134, 135, 148, 216, 220, 224,
 229, 234, 235
 DPI, 439
 Drug binding, 80, 81
 Drug delivery, 58, 64, 66–70, 77, 78, 81, 125,
 131, 136, 147, 160, 259–262, 270, 271,
 280, 281, 411, 412, 414, 415, 417, 422
 Drug discovery, 73, 74, 80
 Drug-drug interactions, 4, 8
 Drug-like, 2, 3, 5
 Drug metabolism, 79
 Drug processing, 58, 59, 64–66
 Drug release and activation, 139, 152–160
 Drug response, 76
 Drug targeting, 133–136, 184, 186, 187
 Drug transport, 79, 81, 103–119
 Drug transporter, 78, 79
 Dry powder inhalers, 3, 5, 7, 439
 Dry powder systems, 17

- E-cadherin, 19, 25
EDTA, 7
Efficacy, 3–8, 76
Efflux, 78, 80
Efflux pump, 22, 23
Electrical resistance, 19
Emphysema, 13
Emulsions, 1, 8
Enalapril, 129
Enalaprilat, 129
Endocytic, 280, 281, 297
Endocytosis (endocytotic), 306, 310, 311, 314
Endosomes, 281
Energy-dependent, 280, 281, 297
Enhancers, 1, 6, 7
E^{ms} Peptide, 286
Enol ester, 150
Enterocytes, 107–108
EO9, 134
Ephedrine, 151
Ester prodrugs, 137–142
Ethylene diamine, 215, 218, 227
Etoposide, 221
Excipient, 63–66
Exclusivity, 436–439
Excretion, 74
Exocytic, 280
Extravasation, 306, 313
- F-Actin, 283
Fibroblast growth factor (FGF), 280, 283, 289–291, 296, 297
Famciclovir, 129
Fatty acids, 7
FDA, 441
Ferredoxin-NADP⁺ reductase, 204
Fexofenadine, 161, 162
FLM5011, 150
Floxuridine (FUDR), 156, 157
Fluorescence, 76
5-Fluorocytosine (5-FC), 212, 227, 230, 236, 237
5-Fluorouracil (5-FU), 212, 227, 230, 236, 237, 238
Fluphenazine, 130
Fluphenazine decanoate, 130
Fluphenazine enanthate, 130
Folate-drug conjugates, 176, 177, 181
Folate receptor, 426
Formulation, 24, 25, 58–60, 62–65, 68, 70
Fosinopril, 141
Fosinoprilat, 141
Fusion, 282–284
- GABA, 290
GDEPT, 135
GF120918, 385, 386, 391, 395–397
Gene delivery, 263, 269–271, 290, 293, 305, 307, 309, 311, 312, 314, 430, 412, 417, 421, 419
Gene-directed enzyme prodrug therapy (GDEPT), 203, 231, 236,
Gene regulation, 77, 79, 80
Gene therapy, 281, 287, 305–307, 309, 312, 314
Glucuronidase, 203, 223, 231
Glycosylation, 10
- Hatch-waxman act, 437, 438
Heat shock protein, 283
Heparan sulfate (HS), 284, 290
Heparin, 282
Herceptin, 364, 372
Hetacillin, 143, 161
High-throughput screening, 74, 78
HIV-1, 283, 284
Homoarginine, 290
Homeodomain, 284
Homeoproteins, 284, 285
Hoxa-5, 285
HSV-1, 281, 290
Hydrodynamics-based procedure, 312, 313
Hydrocortisone, 151, 152
Hydrogen-bonding potential, 23–25
Hydrolysis, 62–64
Hydrophilicity, 127
Hyperthermia, 250, 248
Hypoxia, 203
Hypoxia-selective anticancer agent toxicity, 204, 207, 209
- Ifosfamide, 230, 238
Immunotoxin, 363, 366, 369, 371
Indomethacin, 131
Inhalation, 29
Inhalers, 440
Inhibitors, 1, 6
Immunoconjugate, 363, 366–69
Immunotoxin, 363, 366, 370, 371
Interleukin, 280, 296,
Internalization, 284, 285, 289–291, 297

- In silico, 78, 81
Islet-I, 285
Insulin, 12, 14
Intellectual property, 160
Intestinal mucosa, 16–18, 23
Intracellular, 80
Intramolecular cyclization, 155–160
Intestinal epithelium, 107–109, 113
Ipsalazide, 132
In vitro, 78, 81, 282, 284, 285, 296, 297
In vivo, 282, 284, 285, 296, 297, 307, 309–314
- Kidney, 117–118
- β -Lactamase, 234
Levonorgestrel, 149
Ligand-drug conjugates, 170, 171, 173
Lipinski's rule of 5, 127
Lipophilicity, 127, 128
Liposomal, 14, 29
Liposomal carriers, 363, 374
Liposome, 1, 12, 21, 280, 283, 289, 290, 310, 311, 411, 431, 434
Low pH activated anticancer prodrugs, 213
Lysosomes, 281
- Magnetic resonance imaging, 76
Mannich base, 142–143, 147
MDCK cells, 104, 108, 117–118
MDI, 439
MDR1, 382–385, 396
MDR3, 381, 382, 384, 385, 396–398
Mdr1a/1b(–/–) knockout mice, 387, 388, 392, 396, 397
Mdr1a, 384, 387, 388, 392, 396
Mdr1b, 384, 387, 388, 392
Mecillinam, 128
Mechanism, 250, 252, 253, 258, 261–265, 271
Melfalan, 235
Membrane permeability, 79
Mesalazine, 132, 147
Metabolic barrier, 78
Metabolism, 4, 7–9, 12, 74
Metered dose inhaler, 3, 7, 9, 26
Micelle, 9, 29
Microbubble, 261
Microfilaments, 291
Microtubules, 281, 291
Microvilli, 17
Midodrine, 145
- Microparticle, 29
Microspheres, 29
Mitogenic activity, 283
Mitomycin C, 134, 205, 221, 234, 238
Mitoxantrone, 385, 394, 395
MK571, 385, 391
Molecular chaperones, 283
Molten Globule (MG), 282, 283, 291–294
MRP, 22
MRP1, 382, 385, 390–392, 394
MRP2, 382, 385, 390–396
MRP3, 382, 385, 390–392, 394
MXR, 382, 394
Multidrug resistance-associated proteins (MRPs) 109, 110, 118
MDCK, 25
Multidrug resistance (MDR), 382–384, 386, 390, 391, 395, 397, 398
Mylotarg, 364, 371, 372
- N*-Oxide containing anticancer prodrugs, 208
E5-N-NITROSOUREA, 218
Nabumetone, 142
NADPH-cytochrome P450 reductase, 204, 205, 210
NADH-cytochrome b₅ reductase, 204
NADH:ubiquinone oxidoreductase, 204
NAD(P)H:quinone acceptor oxidoreductase (DT-diaphorase), 204, 237, 238
Naked plasmid DNA, 308, 309, 312–314
Nanoencapsulation, 8
Nanoparticles, 1, 2, 7, 8, 29
Naproxen, 131
Nasal epithelium, 111–112
NCE, 2–5, 8, 9
Nebulizer, 4, 20, 21, 31
Nebulizers, 4, 5, 17, 21, 31
Needless Injections, 30
New chemical entity, 2
Nifedipine, 440
Nitrogen mustards, 206, 207, 211, 216, 226, 227, 233
Nitromin, 209, 211
Nitrophenyl phosphoramides, 135, 154
Nitroreductase, 132, 135, 154, 155, 231, 238
NLS, 281, 283
Non-classical transport, 280, 281, 283, 284, 286, 287, 290, 293, 296, 297
Nonviral, 307, 309–311
Norethindrone, 149
Norgestimate, 149
Novel delivery systems, 28
Nuclear pore, 281
Nuclear localization, 281, 284, 286

- Nuclear transcription, 283
Nucleotidylation, 281
Nucleus, 283
- o*-Aminobenzyl alcohol, 215
Ocular cellular barriers, 114–115
Occludin, 19
Oehlke Peptide, 286
o-Hydroxylbenzyl alcohol, 215, 225
Oligonucleotides, 282
OKT3, 364
Olsalazine, 132, 147
Osmotic Implants, 29
Oral bioavailability, 127–129
Oral delivery, 16
Oral drug delivery, 439
Orthoclone, 364
Oxazolidine, 151
Oxazoline, 151
Oxidation, 62, 63, 64
Oxime prodrug, 149
- p*-Aminobenzyl alcohol, 214, 218, 223
Particulate cargoes, 107–111, 113, 114, 116, 118, 284
p-Glycoprotein (P-gp), 8, 12, 23, 382–390, 394 253
p-Hydroxylbenzyl alcohol, 215, 225
Paclitaxel, 80, 81, 215, 218, 228, 235
Paracellular pathway, 17, 18, 20
Paracellular transport, 6
Patent, 436–441
Paxil, 439
Pegylation, 1, 10, 29
Peyer's patches, 7
Penciclovir, 129
Penetratin, 282, 284, 285, 286, 288–290, 291
Pent term, 437
Pep-1, 286
PepT1, 22
Peptide(s), 280, 282, 284, 285–291, 297
PD, 74, 77–81
Pegylation, 1, 10
PH, 282, 283
Pharmacokinetics, 3–8, 11, 73, 80
Pharmacodynamics, 4, 7, 8, 11, 73, 80
Pharmacophore, 6
Pharmaceutical properties, 136
Pharmacokinetics, 363, 365
Pharmacokinetic profiles, 136
Phospholipids, 424, 411–415
Phosphorylation, 281
Physicochemical properties, 12, 28, 31, 58–60, 63–70
Physicochemical, 75, 77, 79
Pilocarpine, 158, 159
Pivampicillin, 128, 140
Pivmecillinam, 128, 140
PK, 74, 76–81
Placental barrier, 115–116
Plasma concentration, 80
Plasmid, 282, 284, 287, 307–314
Plasmin, 213, 216, 218
Polyanion(s), 282, 283, 290, 291, 293, 297
Polyarginine, 286, 289, 290
Polycations, 280, 285, 297
Polycationic, 280, 281, 284
Polyethelene imine, 280
Polyhistidine, 289
Poly-L-Lysine, 280, 286, 289
Polymer, 280, 311, 313
Polymerization, 414, 415
Polymorphs, 62–65
Polynucleotides, 290
Polyornithine, 289
Polysialic acid, 290
Positron emission tomography, 76
PNA, 282
Preclinical Safety Assessment, 9
Prednicarbate, 140
Preformulation, 6, 8, 11, 15, 30, 31
Prodrug, 363, 366, 371, 373
Proliferation, 283
PreS2-TLM, 286
Preservative, 9, 18
Prodrug design, 136, 137
Prodrug, 24, 25, 60, 62, 64, 125–162, 439–441
Protein, 263, 265, 270, 280–285, 290, 291
Protein transduction domain (PTD), 284, 286–290
Proteoglycans, 283, 284, 290, 296
Pseudomonas exotoxin, 283, 291
Promoiety, 127
Prontosil, 147, 148
Propellants, 15
Proteases, 6, 213
Pulmonary epithelium, 111–114
Pumps, 29
pVEC, 285, 286, 288
- QSPR, 79, 80
Quinone-containing anticancer prodrugs, 205
- Receptor, 283
Receptor affinity, 79, 80

- Receptor-mediated delivery, 78
Receptor-mediated endocytosis, 168, 169, 175, 183
Receptor-targeted therapies, 167, 183
Reductive enzymes, 204
Remicade, 364
Renal excretion, 382, 390, 398
Renal epithelium, 117–118
ReoPro, 112–113, 364
Respiratory airway epithelium, 112–113
Retinal epithelium, 115
Retrovirus, 283
Reversible prodrug form, 137, 138
Rilmazafone, 159
Rituxan, 364
Rolitetracycline, 143
RNA, 285, 291
S-Oxide containing anticancer prodrugs, 211
Salt forms, 63
Schiff base, 148
Secondary structure, 282–284, 291
Secretion, 284, 285, 295
Secretory, 280, 283, 295
Signal peptide, 285
Shelf life, 59
Simulect, 364
Site of action, 74, 76
Site-specific activation, 133–136
Solubilizer, 13
Solubility, 58
Solid state, 58–60, 62
SPGP, 382, 397, 398
Stability, 58
Stabilizer, 13, 14
Statutory bar, 436
Steric stabilization, 414
Stromelysins, 213
Sucrose, 282
Sulfanilamide, 147, 148
Sulfasalazine, 132, 147
SV40 virus, 280
Synagis, 364
Syncytiotrophoblast, 115–116
Systemic circulation, 75, 81

Talampicillin, 128
Targeted bioavailability, 74, 76, 77, 79, 81
Targeted delivery, 424, 412
Tat, 282, 283–290, 297
Terfenadine, 161
Tegafur, 230

Tertiary structure, 282, 284, 291, 296
Tetracycline, 143
Thermostabilizer, 13
Thiazolidine, 151
Tight junctions, 17–19, 24, 25
Tirapazamine, 208
Topotecan, 385, 396, 397
Toxicology, 4, 9
Toxicokinetics, 4
Transduction domain, 363, 374
Transactivating factor, 4
Transcellular, 7
Transcellular pathway, 17, 20
Transdermal, 9
Transdermal drug delivery, 259–262
Transfection, 310, 311, 313, 314
Transgene expression, 307, 309–314
Translocation, 284, 285, 291, 292, 296, 363, 369, 374
Transepithelial electrical resistance (TEER), 110, 112–114, 118
Transport, 77, 78, 281–286, 291, 295–297
Transportan, 286, 289
Transporter, 4, 8, 12, 107–111, 113, 115–118
Tubilin, 81
Tumor hypoxia, 133

Ultrasound, 270, 271
Uptake, 307, 308, 310, 311, 313, 314

Valacyclovir, 129
Vaccines, 281, 282
Variability, 77, 81,
Vesicular transport, 291
Vector(s), 281, 283–290, 292, 293–297
Vehicle(s), 280, 287
Vidarabine, 133
Vinca alkaloid, 234
Vector, 307, 309–313
VP22, 280–282, 287, 289–291, 296

X-ray computed tomography, 76

Zenapax, 364
Zevalin, 364
Zonula Adherens, 18, 19
Zonula Occludens, 18
Zonula occludens toxin, 7