

Index

Page numbers in *italic* refer to illustrations; numbers followed by "t" refer to tables.

- Absorption, 2. *See also* Bioavailability
active, 25
adsorption and, 57-58
bioavailability and, 7-9
biologic considerations affecting, 24-39
buccal, 110-113
capacity-limited transport processes in, 26
 prolonged-release formulations and, 131
carrier-mediated, 25-27, 26
complexation and, 57
dissolution rate-limited, 45-46, 46
dosage form and, 61-79
drug interactions affecting, 306-309
estimating extent of, 8-9
 noncompartmental methods for, 20-21
facilitated, 25
food's effects on, 32-36, 308-309
 with enteric-coated tablets, 69-70, 309
from intramuscular injection, 87-91
from solid dosage forms and suspensions, 45-54
from solution, 40-45
from subcutaneous injection, 91-92
gastrointestinal
 biologic considerations affecting, 24-39
 dosage form and, 61-79
 physicochemical considerations affecting, 40-60
 in thyroid disease, 297, 297
in vitro correlates of, 71-75
membrane physiology in, 24-27
nasal, 102-103
of ionized drug forms, 43-44
passive, 25, 26
percutaneous. *See* Percutaneous absorption
physical-chemical models of, 55-57
physicochemical considerations affecting, 40-60
pulmonary, 95
rate of. *See* Absorption rate
rectal, 114
 drug formulation and, 117
Absorption potential
 calculation of, 55-56
Absorption rate
 concentration-time profile and, 7, 7
 drug concentration and
 for carrier-mediated process, 26, 26
 for passive process, 25, 26
 estimation of, 151-153, 152
Absorption rate constant, 6
 apparent
 gastric emptying and, 31, 31
Accumulation
 during repetitive dosing, 10-11
 prediction of
 method of superposition for, 379, 379t
Acebutolol
 metabolism of
 acetylator status and, 258
Acenocoumarol
 metabolism of, by intestinal flora, 154, 214
Acetaminophen
 absorption of
 gastric emptying and, 29-30, 30-31, 31
 gastric pH and, 47
 in thyroid disease, 297, 297, 298
 cimetidine interaction with, 328-329
 hepatotoxicity of, 219
 pharmacokinetics of
 dose-dependent, 226
 gender differences in, 253
 in obesity, 240
 in thyroid disease, 298
 propoxyphene interaction with, 330
 rectal administration of, 115, 117, 118
Acetazolamide
 binding of, to erythrocytes, 198, 198
 bioequivalence problems with, 161
 prolonged-release formulation of, using elementary
 osmotic pump, 133
Acetylation, 214, 216t
 polymorphic, 256-260
 determining phenotype for, 258, 260
 α_1 -Acid glycoprotein (AAG)
 drug binding to, 195-196, 196, 288
 changes in, in disease, 290, 290
Acidosis
 phenobarbital distribution in, 188
Acyclovir
 prodrug of, 50-51
Administration. *See also* particular routes of
 administration
 continuous
 pharmacokinetics of, 9-13
 routes of, 80
Adsorption
 absorption and, 57-58
Adverse drug reaction(s). *See also* Toxicity
 number of drugs prescribed and, 305, 306
Aerosol(s), 95-97
Age
 body composition changes with
 pharmacokinetic variability due to, 240-242
 pharmacokinetic variability due to, 242t, 242-252
Albumin
 drug binding to, 195, 288
 in liver disease, 289-290
 in renal disease, 288-289, 288-289
 serum level of
 adverse drug reactions and, 293-294
Albuterol
 metabolism of, in gut wall, 158, 229
Alcohol. *See* Ethanol

- Alcoholism
malabsorption due to, 36
- Alkaline diuresis
forced, for drug intoxication, 209
- Alkalosis
phenobarbital distribution in, 188
- Allopurinol
accumulation of metabolite of, in renal disease, 279t
diet's interaction with, 337
dosing interval for, 13
enzyme inhibition by
drug interactions due to, 323-324
rectal administration of, 115
- Alprazolam
propoxyphene interaction with, 330
sublingual administration of, 112-113
- Alprenolol
pentobarbital interaction with, 321
pharmacokinetic variability of, 156, 156t, 236
- Amikacin
implantable infusion system for, 94, 138
individualization and optimization of dosage
regimen for, 351-353
pharmacokinetics of, in obesity, 238
- Amino acid(s)
intestinal transport of, 26
levodopa interaction with, 188-189, 337
- Aminoglycoside(s). *See also* particular drugs
dosage regimens for
adjustment of, in renal disease, 276, 277
individualization and optimization of, 351-353, 352t
pharmacokinetics of, in obesity, 238
toxicity of
plasma concentrations and, 352-353
- Aminophylline, 370
- Aminopyrine
clearance of, in congestive heart failure, 294
oral contraceptives' interaction with, 326
- Aminosalicilate
bioequivalence problems with, 161
- 5-Aminosalicic acid (5-ASA). *See also* Sulfasalazine
rectal administration of, 117
resin-coated, 71
- Amiodarone
digoxin interaction with, 316.
- Amitriptyline
half-life of
charcoal's effect on, 211
individualization and optimization of dosage
regimen for, 367
pharmacokinetics of, in elderly patients, 251
- Amobarbital
pharmacokinetics of
age and, 242t
- Amoxicillin
dosage regimen for
adjustment of, in renal disease, 275
- Amphetamine
adverse reactions to
urine pH and, 311, 312
antacid interaction with, 311
carboxymethylcellulose complexation with, 57
detection of, in urine
sodium bicarbonate and, 208
metabolism of
stereoselectivity in, 222
renal clearance of
urine pH and, 208
- Ampicillin
absorption of
crystal form and, 53
bioequivalence problems with, 161
central nervous system penetration of, 188
changes in gut bacteria due to
bioavailability of other drugs and, 154
competitive inhibition of tubular secretion of, 206
crystalluria due to, 209
in synovial fluid, 197
pharmacokinetic variability of, 234
pharmacokinetics of, in pregnancy, 254
prodrugs of, 42-43
stability of, in gastric fluid, 54
- Amrinone
acetylation of
genetic factors and, 259-260
- Analgesic(s). *See also* particular drugs and classes of
drugs
topical application of, to skin, 106
- Anesthesiology resident(s)
warfarin pharmacokinetics in, 338
- Anesthetic(s). *See also* particular drugs
pharmacokinetics of, in elderly patients, 250-251
- Angiotensin converting enzyme inhibitor(s). *See also*
particular drugs
pharmacokinetics of, in cardiovascular disease, 296
- Antacid(s)
effects of, on urine pH
drug interactions due to, 311
interference of, with absorption of other drugs, 306-307
- Antiarrhythmic agent(s). *See also* particular drugs and
classes of drugs
individualization and optimization of dosage
regimens for, 347-351
pharmacokinetics of, in cardiovascular disease, 295-296
- Antibiotic(s). *See also* particular drugs and classes of
drugs
central nervous system penetration by, 188
changes in gut bacteria due to
bioavailability of other drugs and, 154
digoxin interaction with, 154, 308, 308t
food's effects on absorption of, 33-34
individualization and optimization of dosage
regimens for, 351-353
salivary excretion of, 211
- Anticholinergic agent(s). *See also* particular drugs
interference of, with absorption of other drugs, 307
- Anticoagulant(s). *See also* particular drugs
barbiturate interaction with, 319, 320
individualization and optimization of dosage
regimens for, 364-365
- Anticonvulsant(s). *See also* particular drugs
bioequivalence of generic products, 159-160
enzyme induction by
drug interactions due to, 317-321
hypersensitivity to, 219
individualization and optimization of dosage
regimens for, 353-359
pharmacokinetics of, in pregnancy, 254-255
treatment with, during pregnancy
congenital malformations and, 219-220
- Antidepressant(s). *See* Tricyclic antidepressant(s)
- Anti-inflammatory drug(s). *See* Nonsteroidal anti-
inflammatory drug(s); particular drugs
- Antinuclear antibody(-ies)
with hydralazine therapy
acetylation phenotype and, 259
with procainamide therapy
acetylation phenotype and, 258-259, 259

- Antipsychotic drug(s). *See* Neuroleptic(s); particular drugs
- Antipyrine
 osmotic rectal delivery of, 142
 pharmacokinetics of
 allopurinol's effects on, 324
 anticonvulsants' effects on, 318
 as indicator of hepatic drug metabolism, 287
 beta-blockers' effects on, 326
 calcium channel blockers' effects on, 329
 diet's effects on, 336
 disulfiram's effects on, 323
 in elderly patient, 247
 in liver disease, 281, 281-282, 282t
 in thyroid disease, 298
 insecticides' effects on, 337-338
 oral contraceptives' effects on, 253, 326-327
 propoxyphene's effects on, 330
 twin studies of, 256, 256t
 with elevated body temperature, 298
- Ara-C
 enzyme inhibition with, 217
- Area under the curve (AUC), 8
 bioavailability estimation from, 146-147
 with concentration-dependent plasma protein binding, 197
 estimation of, 8
 for metabolite, 220
 trapezoidal rule for, 377, 377t, 378
- partial
 estimation of, 8-9
- Area under the first moment curve (AUMC), 17, 17-18
- Arene oxide(s)
 in anticonvulsant hypersensitivity, 219
- Ascorbic acid
 bioavailability of
 dose and, 26-27
 problems with, 161-162
- Aspirin. *See also* Salicylate
 absorption of
 dissolution-rate limited, 46
 gastric pH and, 47
 site of, 27
 aluminum salt of, 50
 bioequivalence problems with, 161
 buffered
 dissolution rate of, 50
 diuretics' interaction with, 313
 enteric-coated
 absorption of, 68-69, 69, 69-70
 food's effect on absorption of, 309
 in enteric-coated granules
 absorption of, 70
 intestinal metabolism of, 229
 pharmacokinetics of
 concentration-dependent, 225
 time-dependent, 227
 rectal administration of, 115, 117
 renal clearance of
 urine pH and, 208
 tenoxicam interaction with, 310
- Atenolol
 pharmacokinetics of
 age and, 249
- Atropine
 individual differences in response to, 176, 176
 topical application of, to eye
 systemic absorption after, 100-101
- Attapulgite
 drug adsorption by, 57-58
- Autoinduction, 216-217, 321-322
 time-dependent kinetics due to, 227, 227
- Bacampicillin, 42-43
- Barbiturate(s). *See also* particular drugs
 absorption of sodium salts of, 49
 anticoagulant interaction with, 319, 320
 enzyme induction by
 drug interactions due to, 320-321
 intranasal application of, 102
- Bayesian forecasting, 350
- Benoxaprofen
 bioavailability of
 particle size and, 51-52
 metabolism of
 stereoselectivity in, 222
- Benzanthine penicillin G
 intramuscular injection of
 prolonged-release formulation for, 136
- Benzodiazepine(s). *See also* particular drugs
 binding of
 intersubject variability in, 197
 cimetidine interaction with, 328, 328t
 pharmacokinetics of
 gender differences in, 253
- Benzoic acid
 dissolution of
 pH-dependent, 47
 rate of, 49t
 trisodium phosphate with
 dissolution rate of, 50
- Benzylpenicillin
 tubular secretion of, 206
- Beta-blocker(s). *See also* particular drugs
 enzyme inhibition by
 drug interactions due to, 326
 pharmacokinetics of
 genetic factors and, 262
- Betamethasone 17-benzoate
 percutaneous absorption of, 107, 107
- Betamethasone dipropionate
 topical
 bioequivalence problems with, 172
- Betamethasone valerate
 topical
 bioequivalence problems with, 172
- Betaxolol
 topical application of, to eye, 101
- Bile
 effects of, on dissolution, 52
- Bile salt(s)
 drug complexation with, 57
 gastric mucosal injury due to
 protective role of unstirred layer for, 44-45
 insulin absorption and, 104-105
 nasal drug absorption and, 103, 104-105
- Biliary excretion, 209-211
 drug interactions involving, 316-317
- Bilirubin
 elevated, in neonate
 phenobarbital in treatment of, 320
 plasma protein binding of drugs and, 244
- Binding
 apparent volume of distribution and, 2, 194-195
 disease's effects on, 288-294
 clinical significance of, 292-294, 294
 pharmacokinetic implications of, 290-292
 drug concentration and, 22-23
 in blood, 195-201

- Binding (cont'd.)**
 in body fluids
 drug concentration and, 187
 in brain, 189
 in tissues. *See* Tissue binding
 irreversible, 199, 199
 plasma protein
 age-related changes in, 248
 alterations of, in liver disease, 289-290
 clearance and, 23, 291
 concentration-response relationship and, 180-181
 disease's effects on, 288-290
 distribution and, 197-199
 diurnal variations in, 197
 drug effects and, 199
 drug interactions involving, 309-310
 elimination and, 200, 200-201
 glomerular filtration and, 203, 204
 in neonate, 244, 244t
 in pregnancy, 253-254
 in renal disease, 288-289
 intersubject variability in, 197
 plasma concentration and, 22-23, 196-197
 renal clearance and, 205-206
 to erythrocytes, 198-199, 198-199
- Bioavailability, 7-9, 146-175. *See also* Absorption**
 absolute (systemic)
 defined, 116
 estimation of, 146-147
 relative vs., 8
 absorption potential as predictor of, 55-56
 canine model for
 problems with, 48
 defined, 7, 146
 dose and
 carrier-mediated transport's effects on, 26-27
 estimation of, 146-151
 from stable isotope studies, 150-151
 from steady-state studies, 149, 150
 factors affecting, 148-149
 hepatic extraction ratio and, 155-156
 intestinal motility and, 32
 intrasubject variability in, 149-151
 of nonoral medications, 171-172
 of topical medications, 108-110, 171-172
 preabsorptive hydrolysis and metabolism and, 153-154
 presystemic metabolism and, 154-158, 155
 regulatory and clinical considerations involving, 158-161
 relative
 absolute vs., 8
 estimation of, 147-151, 148
- Bioequivalence**
 defined, 8
 trials of, 159
- Biotransformation. *See* Metabolism**
- Bismuth subsalicylate**
 interference of, with absorption of other drugs, 307
- Bleomycin**
 continuous vs. intermittent administration of, 125
- Blood**
 binding in, 195-201. *See also* Binding
 concentration in. *See also* Plasma concentration
 estimation of, 23
 distribution in, 187
- Blood flow**
 distribution and, 192, 192-194
 gastrointestinal
 absorption and, 28
 hepatic, 155
 age and, 249, 249
 control of, for intrahepatic chemotherapy, 83-84
 drug interactions involving changes in, 331-333
 drug metabolism in liver disease and, 284-285
 renal
 drug interactions involving changes in, 316
- Blood-brain barrier, 188**
 disruption of
 controlled, 189-190
 in meningitis, 158
 osmotic, 189-190
- Body composition**
 age-related changes in, 241-242
- Body size**
 pharmacokinetic variability due to, 236-242
- Body surface area**
 calculation of, 240-241
 dose estimation for children using, 240-241
- Body weight**
 ideal, 237
 pharmacokinetic variability due to, 236-242
- Body weight-height index**
 response to buttock injection of hepatitis B vaccine and, 88
- Boric acid**
 topical application of
 systemic absorption after, 109
- Brain**
 binding in, 189
 drug penetration to, 188-190
 tumors of
 intra-arterial drug administration for, 84-85
- Bronchodilator(s). *See also* particular drugs**
 inhalation of
 intravenous administration vs., 96
 spacers for use with, 97
 nebulized, 97
- Buccal administration, 110-113**
 disintegration test for tablets for, 73
 prolonged-release formulations for, 142
- Bumetanide**
 pharmacokinetics of, in cardiovascular disease, 296-297
- Bupivacaine**
 propranolol interaction with, 326
- Burn injury**
 pharmacokinetic variability due to, 299-300
- Buserelin**
 intranasal application of, 104
- Buspiron**
 pharmacokinetics of, in liver disease, 286
- Caffeine**
 acetylation phenotype determination using, 260
 hepatic blood flow alterations due to
 drug interactions involving, 332
 methoxsalen interaction with, 331
 pharmacokinetics of
 age and, 243, 243-244
 in smokers, 335-336
- Calcitonin**
 intranasal application of, 105
- Calcium**
 tetracycline complexation with, 33-34, 57
- Calcium carbonate**
 absorption of
 gastric pH and, 47-48
- Calcium channel blocker(s). *See also* particular drugs**
 enzyme inhibition by

- drug interactions due to, 329-330
- pharmacokinetics of
 - age and, 249-250
- Calcium citrate
 - absorption of
 - gastric pH and, 47
- Cancer. *See also* Cancer chemotherapy
 - lung
 - debrisoquin oxidation phenotype and, 261-262
- Cancer chemotherapy
 - drug delivery to central nervous system in, 189-190
 - infusion pump for, 94-95
 - intestinal damage due to
 - drug absorption and, 36-37
 - intra-arterial, 82-85
 - intraperitoneal, 86-87
- Capacity-limited process, 26
- Capsule(s)
 - hard gelatin
 - biopharmaceutic characteristics of, 63-64, 64
 - disintegration test for, 73
 - soft elastic
 - biopharmaceutic characteristics of, 64-65
- Captopril
 - food's effects on absorption of, 33, 308, 308
- Capuride
 - delayed absorption of, with food, 308
- Carbamazepine
 - autoinduction by, 216-217, 321
 - time-dependent kinetics due to, 227, 227
 - bioavailability problems with, 162
 - calcium channel blockers' interaction with, 329-330
 - enzyme induction by, 318
 - drug interactions due to, 321
 - erythromycin interaction with, 330
 - hypersensitivity to, 219
 - in cerebrospinal fluid, 197
 - individualization and optimization of dosage
 - regimen for, 353-355
 - isoniazid interaction with, 323-326
 - pharmacokinetics of
 - age and, 242t, 243
 - charcoal's effect on, 211
 - time-dependent, 227, 227
 - therapeutic concentration range for, 180t
 - seizure type and, 358
- Carbenicillin
 - dosage regimen for
 - adjustment of, in renal disease, 276
 - pharmacokinetics of, with hemodialysis, 278
 - prodrug of, 42
- Carbidopa
 - enzyme inhibition by, in levodopa therapy, 217
- Carboxymethylcellulose
 - amphetamine complexation with, 57
- Cardiac glycoside(s). *See also* particular drugs
 - individualization and optimization of dosage
 - regimens for, 361-363
- Cardiovascular disease
 - pharmacokinetic variability due to, 294-297
- Carmustine (BCNU)
 - hepatic arterial injection of, with starch
 - microspheres, 84
- Carprofen
 - metabolism of, 222
- Carrier-mediated transport, 25-27, 26
- Cefazolin
 - elimination rate constant of
 - creatinine clearance and, 274, 275
 - volume of distribution of, 195
- Cefixime
 - renal clearance of
 - plasma protein binding and, 206
- Ceftriaxone
 - free fraction of, 196-197
 - pharmacokinetics of
 - age and, 242
 - probenecid interaction with, 311-312
- Cefuroxime
 - pharmacokinetics of, in pregnancy, 254
 - prodrug of, 42-43
- Cefuroxime axetil, 42-43
- Celiac disease
 - drug absorption in, 37
- Cell(s)
 - drug distribution into, 187-188
- Cellulose acetate phthalate
 - for enteric coating, 68
- Central compartment, 14, 15
 - apparent volume of
 - calculation of, 16
- Central nervous system. *See also* Brain
 - drug penetration to, 188-190
- Cephacetrile
 - intramuscular injection of, 88-89
- Cephalexin
 - cimetidine interaction with, 313
 - dosage regimen for
 - adjustment of, in renal disease, 275
 - pharmacokinetics of, with hemodialysis, 278
- Cephaloridine
 - furosemide interaction with, 314
 - intramuscular injection of, 88-89
- Cephalosporin(s). *See also* particular drugs
 - probenecid interaction with, 311
- Cephalothin
 - central nervous system penetration of, 185
 - intramuscular injection of
 - complications of, 91
- Cephadrine
 - intramuscular injection of, 89, 89t
 - pharmacokinetics of, in pregnancy, 254
 - tubular secretion of, 206
- Cerebrospinal fluid
 - drug concentration in, 187, 197
 - plasma concentration and, 189
- Charcoal
 - drug adsorption by, 57-58
 - in enterohepatic cycling studies, 211
- Child(ren)
 - pharmacokinetics in, 240-241, 245
- Chloral hydrate
 - warfarin interaction with, 310
- Chloramphenicol
 - bioavailability of
 - after intravenous injection of prodrug, 82, 171
 - after oral administration of prodrug, 53, 54
 - bioequivalence problems with, 162, 162
 - enzyme inhibition by
 - drug interactions due to, 323, 323
 - pharmacokinetics of
 - age and, 243
 - rifampin interaction with, 322
 - topical application of, to eye, 100
 - systemic absorption after, 100
- Chloramphenicol palmitate
 - absorption of
 - crystal form and, 53
 - conversion of, to chloramphenicol, 54

- Chloramphenicol stearate
conversion of, to chloramphenicol, 54
- Chloramphenicol succinate
intravenous injection of
chloramphenicol bioavailability after, 82, 171
- Chlordecone intoxication
cholestyramine for, 211
- Chlordiazepoxide
adverse reactions to
serum albumin and, 293
alcohol interaction with, 334
binding of
intersubject variability in, 197
cerebrospinal fluid-plasma concentration ratio for, 189
cimetidine interaction with, 328, 328t
disulfiram interaction with, 323
intramuscular injection of, 89, 89
pharmacokinetics of
age and, 248
in liver disease, 283
smoking and, 334-335
volume of distribution for, 195
- Chlorothiazide
bioavailability of
intestinal motility and, 32
bioequivalence problems with, 162
colestipol adsorption of, 58
food's effects on absorption of, 34
- Chlorpheniramine
renal clearance of
urine flow rate and, 209
- Chlorpromazine
plasma protein binding of, in disease, 290
prolonged-release formulation of
bioavailability of, 135
propranolol interaction with, 325, 326
- Chlorpropamide
bioequivalence problems with, 162-163, 163
saliva/plasma concentration ratio for, 212
- Chlorthalidone
absorption of
crystal form and, 53
binding of, to erythrocytes, 198
pharmacokinetic variability of, 235
- Cholestasis
pharmacokinetic variability due to, 286
- Cholestyramine
coated with cellulose acetate phthalate, 71
drug adsorption by, 58, 307
in enterohepatic cycling studies, 210-211
phenprocoumon interaction with, 317
- Cilastatin
enzyme inhibition by, in imipenem therapy, 217
- Cilia
nasal
drugs' effects on, 102-103
- Cimetidine
effects of, on tubular secretion
drug interactions due to, 312-313
enzyme inhibition by, 217
drug interactions due to, 327-329, 328t-329t
hepatic blood flow alteration by
drug interactions due to, 332
interference of, with absorption of other drugs, 307-308
pharmacokinetics of
after burn injury, 300
in elderly patients, 246
in liver disease, 283
in obesity, 239
renal excretion of, 276
signs of estrogen excess due to, 329
stereoselective interactions due to, 333
- Ciprofloxacin
theophylline interaction with, 330
- Clearance, 18-19
body weight and, 237
calculation of, for metabolite, 220
defined, 18
free drug, 23
half-life and, 19
hepatic, 155
plasma protein binding and, 23, 200, 200, 205-206
in disease, 291
renal, 204-206
free plasma concentration and, 200, 205-206
total
creatinine clearance and, in renal disease, 274
variability in
correction for, in bioavailability studies, 149-150
- Clofibrate
accumulation of metabolite of, in renal disease, 279t
metabolism of, in renal disease, 279
steady-state plasma concentrations of, in renal disease, 293
- Clonazepam
carbamazepine interaction with, 321, 321
phenytoin interaction with, 319
- Clonidine
transdermal, 141
- Clorazepate, 50, 218
conversion of, to nordiazepam
gastric fluid pH and, 54
- Cloxacillin
in synovial fluid, 197, 198
tubular secretion of, 206
- Coating dissolution time
absorption of enteric-coated tablets and, 68
- Cocaine
concentration-response relationship for, 181, 182
time course of effect of, 184, 184
- Colestipol
drug adsorption by, 58, 307
- Compartment(s)
rapidly equilibrating (central), 2
slowly equilibrating (peripheral), 2
- Complexation, 57
- Compression
in tablet production, 65
effects of, on bioavailability, 66-67
- Concentration
absorption rate and
for carrier-mediated process, 26, 26
for passive process, 25, 26
plasma. *See* Plasma concentration
- Concentration-response relationship(s), 176-186
factors complicating, 180-183
quantitative models of, 177-178, 177-179
- Concentration-time profile, 3
absorption rate and, 7, 7
after extravascular administration, 6, 6-7
after intravenous bolus administration, 3-4, 4
with multicompartmental pharmacokinetics, 14, 14
after long-term constant rate infusion, 9, 10
after repetitive oral administration, 10-11, 11
after short-term constant rate infusion, 5, 5
area under. *See* Area under the curve
during dosing interval
limitations of noncompartmental analysis for, 21-22
first moment of, 17

- patient-to-patient variability in, 7
- postabsorptive phase of, 6
- zero moment of, 17
- Congestive heart failure
 - effects of, on drug metabolism, 294
 - implantable infusion system for dobutamine for, 94, 138
- Conjugation, 214, 216†
- Contraceptive(s)
 - implants of, 137, 138
 - intramuscular depot preparations of, 137
 - oral
 - anticonvulsants' effects on pharmacokinetics of, 318, 320
 - drug interactions due to enzyme inhibition by, 253, 326-327
 - rifampin interaction with, 322
- Controlled-release medication. *See* Prolonged-release medication
- Corticosteroid(s). *See also* particular drugs
 - inhalation of, 96-97
 - rectal administration of; 117
 - rifampin interaction with, 322
 - topical
 - bioavailability of, 171-172
 - systemic absorption of, 109
- Corticosteroid-binding globulin
 - drug binding by, 196
- Cosolvent(s)
 - in solution preparation, 62
- Creatine phosphokinase (CPK)
 - serum elevation of, after intramuscular injection, 91
- Creatinine
 - serum
 - renal function assessment from, 278-279
- Creatinine clearance, 204
 - as renal function indicator
 - serum creatinine vs., 278-279
 - in renal disease, 272-273
 - measurement of, 272
- Cromolyn
 - inhalation of, 96
- Crystal form
 - dissolution and, 53-54
- Crystalluria, 209
- Cyclophosphamide
 - active metabolite of, 218
 - dexamethasone interaction with, 217, 322
 - enzyme induction by, 217, 321-322
- Cyclosporine
 - absorption of
 - bile and, 52
 - in malabsorptive states, 37
 - binding of, to erythrocytes, 198
 - erythromycin interaction with, 530
 - individualization and optimization of dosage regimen for, 363
 - pharmacokinetics of
 - age and, 242
- Cyproheptadine
 - toxicity of, 219
- Cystic fibrosis
 - pharmacokinetic variability due to, 300-301
- Cytarabine
 - enzyme inhibition with, 217
- Dapsone
 - acetylation of
 - genetic factors and, 258
 - half-life of
 - charcoal's effect on, 211
- DDT
 - antipyrine half-life and, 338
- Debrisoquin
 - oxidation of
 - genetic factors and, 260-262
 - mephenytoin hydroxylation phenotype and, 265
 - screening technique for drugs that cosegregate with, 333-334
- Deet (diethyltoluamide)
 - systemic absorption of, 109
- 6-Deoxyacyclovir, 50-51
- Dermis, 105-106
- Desciclovir, 50-51
- Desipramine. *See also* Imipramine
 - antipsychotic agent interaction with, 326
 - individualization and optimization of dosage regimen for, 368
 - pharmacokinetic variability of, 235
 - pharmacokinetics of
 - genetic factors and, 264
 - in elderly patients, 251
- Desmethyldiazepam. *See* Nordiazepam
- Desmopressin
 - intranasal application of, 104
- Desoxycorticosterone pivalate
 - intramuscular injection of
 - prolonged-release formulation for, 136
- Dexamethasone
 - cyclophosphamide interaction with, 217, 322
 - placental transfer of, for congenital adrenal hyperplasia prevention, 192
 - topical application of, to eye, 98
- Dexamethasone acetate
 - intramuscular injection of
 - prolonged-release formulation for, 136
- Dexamethasone phosphate
 - intravenous injection of, 82
- Dexamethasone sulfate
 - intravenous injection of, 82
- Dextran
 - nasal absorption of, 103
- Dextromethorphan
 - debrisoquin oxidation phenotype determination using, 261
- Diabetes mellitus
 - insulin-infusion pump for, 93-94, 138
- Diazepam
 - active metabolites of, 218
 - adverse reactions to
 - serum albumin and, 293
 - anticonvulsants' interaction with, 318
 - binding of
 - in liver disease, 289
 - in neonate, 244, 244†
 - in renal disease, 289
 - intersubject variability in, 197
 - bioequivalence problems with, 163
 - cimetidine interaction with, 328, 328†
 - dissolution and absorption of
 - pH and, 47
 - disulfiram interaction with, 323
 - excretion of, in milk, 212-213
 - intramuscular injection of, 90
 - intravenous injection of, 80
 - omeprazole interaction with, 331
 - oral contraceptives' interaction with, 327
 - pharmacokinetics of
 - age and, 242†, 244†, 248, 248

- Diazepam, pharmacokinetics of (*cont'd.*)
 dose-dependent, 226
 genetic factors and, 266
 in liver disease, 282-283, 283t
 in renal disease, 291
 propoxyphene interaction with, 330
 rectal administration of, 116
 rifampin interaction with, 322
 smoking and, 334-335
- Dicalcium phosphate
 as filler in tetracycline dosage form, 57, 64
- Diclofenac
 lithium interaction with, 313
- Dicumarol
 allopurinol interaction with, 324
 chloramphenicol interaction with, 323
 pharmacokinetics of
 twin studies of, 256, 256t
 phenobarbital interaction with, 320
- Diet
 enzyme induction by, 317, 336
 pharmacokinetic variability due to, 336-337
- Diethyltoluamide (deet)
 systemic absorption of, 109
- Diffusion
 facilitated, 25
 passive, 25, 26
 carrier-mediated transport with, 26
- Diffusion layer, 46
 pH of
 dissolution and, 48
- Diflunisal
 clearance of
 plasma protein binding and, 200
- Diflunisal
 metabolism of, in renal disease, 279
- Digitoxin
 dissolution of
 bioavailability and, 77t, 77-78
 enterohepatic cycling of, 210
 individualization and optimization of dosage
 regimen for, 363
- Digoxin
 absorption of
 from soft elastic capsules, 64-65
 from tablets, 66
 in malabsorptive states, 36, 37
 in thyroid disease, 297
 intragastric hydrolysis and, 54
 model of, 56-57
 amiodarone interaction with, 316
 antibiotics' interaction with, 154, 308, 308t
 apparent volume of distribution of, in disease, 291
 bioavailability of
 during pregnancy, 254
 particle size and, 51
 bioequivalence problems with, 163-164, 164
 calcium channel blockers' interaction with, 316, 329
 cholestyramine interaction with, 58, 307
 concentration-response relationship for, 182
 dosage regimen for
 adjustment of, in renal disease, 276, 292
 individualization and optimization of, 361-363, 362t
 hydroquinone complexation with, 57
 intramuscular injection of, 90-91
 kaolin-pectin interaction with, 307
 loading with, 12
 pharmacokinetics of
 age and, 244, 244t, 245
 in elderly patients, 246
 in obesity, 238
 in pregnancy, 254
 in thyroid disease, 297-298
 preabsorptive metabolism of, 153-154, 154, 214
 oral antibiotics' effects on, 154, 308, 308t
 quinidine interaction with, 314-315, 314-316
 renal clearance of
 intersubject vs. intrasubject variability in, 235
 therapeutic concentration range for, 180t
 tissue binding of, in renal disease, 290
 vasodilator interaction with, 316, 317t
 verapamil interaction with, 316, 329
- Dilevalol, 223-224
- Diltiazem
 enzyme inhibition by
 drug interactions due to, 329-330
- Diluent(s)
 in capsule dosage forms, 64, 64
 in direct compression tablets, 65
- Dimethyl sulfoxide (DMSO)
 blood-brain barrier disruption by, 189
 in topical formulations, 107
- Dinoprostone
 intravaginal application of, 101-102
- Dipyridamole
 absorption of
 from tablets, 66, 66
 pH and, 47
 dissolution of
 pH and, 47
- Direct compression
 tablet production by, 65
- Disease. *See also* particular types of disease
 pharmacokinetic variability due to, 272-304
- Disintegration
 of tablet, 65, 66
- Disintegration test(s), 71-74
 results of
 absorption and, 73-74
- Disopyramide
 free fraction of, 196
 intravenous administration of
 dosing scheme for, 81
 prolonged-release formulation of, 131
 therapeutic concentration range for, 180t
- Disposition, 137-233. *See also* Distribution; Elimination
 defined, 187
 of metabolites, 220
- Dissociation constant (pKa)
 absorption and, 40-41
- Dissolution, 45-46
 crystal form and, 53-54
 diffusion layer pH and, 48
 of salts, 48-50, 49t
 of tablet, 65, 65-67
 pH and, 46-48
 surface area and, 51-53
- Dissolution rate
 factors affecting, 46
- Dissolution test(s), 74-78, 75
 bioequivalence and, 159
 results of
 absorption and, 76-78
- Dissolution time
 for enteric coating, 68
- Distribution, 2, 187-202
 blood flow and, 192, 192-194
 cellular, 187-188
 defined, 1
 in blood and other fluids, 187
 into central nervous system, 188-190

- of metabolites, 220
- plasma protein binding and, 197-199
- stable isotope studies of, 193-194
- volume of. *See* Volume of distribution
- Distribution equilibrium
 - multicompartmental data analysis at, 16-17
- Distribution half-life
 - estimation of, 193-194
- Disulfiram
 - enzyme inhibition by
 - drug interactions due to, 323
- Diuretic(s)
 - anti-inflammatory drugs' interaction with, 313
 - loop
 - pharmacokinetics of, in cardiovascular disease, 296-297
- Dobutamine
 - implantable infusion system for, 94, 138
- Dog(s)
 - as model for bioavailability studies
 - problems with, 48
 - gastrointestinal pH in, 48
- Dopamine
 - prodrug of. *See* Levodopa
- Dosage form(s). *See also* Capsule(s); Solution(s); Suspension(s); Tablet(s)
 - absorption and, 61-79
 - food's effects on, 33
 - biopharmaceutic characteristics of, 62-71
 - Dosage regimen(s), 344-376
 - adjustments to, in renal disease, 275-277
 - individualization of, 344
 - clinical experience with, 347-371
 - optimization of, 344-347
 - clinical experience with, 347-371
- Dose
 - loading. *See* Loading dose
 - proportionality, 2
 - response relationship
 - individual variability in, 176, 176
 - Dosing interval, 12-13
 - concentration-time profile during
 - limitations of noncompartmental analysis for, 21-22
 - therapeutic index and, 125
- Doxepin
 - propoxyphene interaction with, 330
- Doxorubicin
 - active metabolite of, 218-219
 - implantable infusion pump for, 138
- Doxorubicinol, 218-219
- Doxycycline
 - bismuth subsalicylate interaction with, 307
 - ferrous sulfate interaction with, 306
- Drug interaction(s)
 - drug categories associated with, 305-306, 306
 - pharmacokinetic variability due to, 305-343
- Drug therapy
 - steps in initiation and management of, 345
- Duration of effect, 183-185, 183-186
 - determinants of, 124-125
 - redistribution and, 192
- Dyazide (hydrochlorothiazide/triamterene), 165. *See also* under Hydrochlorothiazide
- Dyphylline, 370
- Effect(s). *See* Response
- Elderly patient(s)
 - guidelines for clinical investigation of drugs for use by, 252
- pharmacokinetics in, 241-242, 246-252
- Elementary osmotic pump (EOP), 132-133, 132-134
- Elimination, 2, 203-233. *See also* Excretion; Metabolism
 - concentration-dependent, 224-226, 225
 - defined, 1
 - in elderly patients, 246-252
 - in renal disease, 273-275, 273-275
 - of metabolites, 220
 - plasma protein binding and, 200, 200-201
 - Elimination rate, 18
 - Elimination rate constant, 3
 - calculation of, 4
 - creatinine clearance and, in renal disease, 274, 274-275
- Enalapril, 43
 - food's effects on absorption of, 33
 - pharmacokinetics of
 - in cardiovascular disease, 296
 - in elderly patients, 246
 - in liver disease, 284
 - in renal disease, 276
- Enalaprilat. *See also* Enalapril
 - pharmacokinetics of
 - in elderly patients, 246
 - in renal disease, 276
- Encainide
 - active metabolites of, 218
 - pharmacokinetics of
 - genetic factors and, 262-263
 - in liver disease, 286
 - in renal disease, 280
- Enflurane
 - renal toxicity of, 219
- Enoxacin
 - enzyme inhibition by
 - drug interactions due to, 330
- Enteric-coated granule(s), 70
- Enteric-coated tablet(s)
 - biopharmaceutic characteristics of, 68-71
 - disintegration test for, 73
 - gastric emptying of, 29
 - lag time for
 - gastric residence time and, 309
- Enterohepatic cycling, 209
 - detection of, 210-211
- Environmental chemical(s)
 - pharmacokinetic variability due to, 334-338
- Enzyme induction, 216-217. *See also* Autoinduction
 - by diet, 336
 - drug interactions due to, 317-323
 - smoking's effect on
 - age and, 249
- Enzyme inhibition, 217
 - drug interactions due to, 323-331
- Ephedrine
 - absorption of, 43, 43
 - renal clearance of
 - urine pH and, 208
- Epidermis, 105
 - drug metabolism in, 228
- Epidural administration, 85-86
- Epilepsy
 - plasma α_1 -acid glycoprotein concentrations in, 290
- Epinephrine
 - in subcutaneous injections, 91
- Equilibrium distribution ratio, 193
- Ergotamine
 - sublingual administration of, 113
- Erythrocyte(s)
 - drug binding to, 198-199, 198-199

- Erythromycin
 changes in gut bacteria due to
 bioavailability of other drugs and, 154
 digoxin interaction with, 154, 308
 enzyme inhibition by
 drug interactions due to, 330
 food's effects on absorption of, 33
 gastric degradation of, 52-53, 54
 prodrugs of
 problems with conversion of, 54-55
- Erythromycin base
 bioavailability of, 54
 enteric-coated products of
 bioavailability of, 55
- Erythromycin estolate
 conversion of, to erythromycin, 54-55
- Erythromycin ethylsuccinate
 conversion of, to erythromycin, 54-55
 food's effects on absorption of, 34
- Erythromycin propionate
 gastric degradation of, 52-53
- Erythromycin stearate
 bioavailability of, 55
- Esophageal transit
 delays in
 drug absorption and, 30
- Esophageal ulceration
 due to drugs lodging in esophagus, 30
- Estradiol
 brain-selective delivery of, 190
 hepatic metabolism of
 smoking's effects on, 216, 336
 intramuscular injection of
 prolonged-release formulation for, 137
 topical application of
 hydroalcoholic gel for, 110
 transdermal system for, 141-142
- Ethanol
 enzyme induction by, 317
 gastric absorption of, 27
 pharmacokinetic variability due to, 334
 pharmacokinetics of
 age-related changes in, 241, 242
- Ethinyl estradiol
 presystemic metabolism of, 158
- Ethosuximide
 carbamazepine interaction with, 321
 individualization and optimization of dosage
 regimen for, 355
 valproic acid interaction with, 327, 327t
- Ethotoin
 concentration-dependent elimination of, 225
- Etomidate
 intravenous infusion of
 dosing scheme for, 81
- Etretinate
 food's effects on absorption of, 35
- Excretion, 203-213
 biliary, 209-211
 drug interactions involving, 316-317
 drug interactions involving, 310-317
 in milk, 212-213
 renal. *See* Renal excretion
 salivary, 211-212
 urinary. *See* Urinary excretion
- Extracellular water
 age-related changes in, 241
 drug distribution in, 187
 estimation of volume of, 194
- Extraction ratio, 18
- hepatic, 155-156
 pulmonary, 193
- Extravasation
 with intravenous infusion, 82
- Extravascular administration. *See also* particular routes
 of administration
 plasma concentration after, 5-6, 6
- Eye
 topical application to, 97-101
 age and, 100
 intravenous injection vs., 100
 prolonged-release formulations for, 138-139
 systemic absorption from, 100-101
- Famotidine
 dosage regimen for
 adjustment of, in renal disease, 276
- Felodipine
 anticonvulsants' interaction with, 319
 pharmacokinetics of
 age and, 250
- Fenopropfen
 enteric-coated
 absorption of, 69
 metabolism of
 stereoselectivity in, 222
- Fentanol
 buccal aerosol administration of, 112
- Fentanyl
 continuous vs. intermittent infusion of, 126
- Ferrous sulfate
 tetracycline interaction with, 306
- Fick's first law, 25
- Film-coated tablet(s), 67
- First moment of concentration-time curve, 17
- First-order kinetics, 3-4, 4
- First-pass effect. *See* Presystemic metabolism
- Flecainide
 individualization and optimization of dosage
 regimen for, 350-351
 pharmacokinetics of
 genetic factors and, 264-265
 in liver disease, 284
 renal clearance of
 urine pH and, 208
- Floxuridine (FUDR)
 hepatic arterial infusion of, 83
 with starch microspheres, 84
- Flucytosine
 half-life of
 creatinine clearance and, 275, 275
- Fludrocortisone
 absorption of
 crystal form and, 54
- Fluocinolone acetoneide
 percutaneous absorption of, 106
- Fluoride
 tubular reabsorption of, 209
- Fluorometholone
 topical application of, to eye, 99, 99
- 5-Fluorouracil (5-FU)
 hepatic arterial infusion of, 83
 intestinal transport of, 26
 intraperitoneal administration of, 87, 94-95
 malabsorption due to, 36
- Fluoxetine
 pharmacokinetics of, in liver disease, 283-284
- Fluphenazine decanoate
 imipramine interaction with, 326

- intramuscular injection of
 - prolonged-release formulation for, 136-137
 - Fluphenazine enanthate
 - intramuscular injection of
 - prolonged-release formulation for, 136
 - Flurazepam
 - presystemic metabolism of, 158
 - Flurbiprofen
 - buccal absorption of, 110-111
 - Food. *See also* Diet
 - effects of, on drug absorption, 32-36, 308-309
 - with enteric-coated tablets, 69-70, 309
 - prolonged-release medication and, 134-135, 135
 - Free fraction
 - in blood
 - calculation of, 23
 - in plasma
 - determination of, 23
 - total concentration and, 196-197
 - Furadantin (nitrofurantoin), 166. *See also* Nitrofurantoin
 - Furosemide
 - absorption of, 153
 - apparent volume of distribution of, in disease, 291
 - bioequivalence problems with, 164-165
 - effects of, on renal function
 - drug interactions due to, 314
 - pharmacokinetics of
 - in cardiovascular disease, 296-297
 - moment analysis of, 20-21
 - plasma protein binding of
 - in liver disease, 290
 - in renal disease, 289, 289
 - Galactose
 - clearance of, as indicator of hepatic drug metabolism, 287
 - Gamma benzene hexachloride. *See* Lindane
 - Gastric emptying
 - drug absorption and, 29-31, 30-32
 - from enteric-coated tablets, 68, 69-70
 - Gastric fluid
 - pH of, 28-29
 - Gastric residence time
 - lag time for enteric-coated tablets and, 309
 - Gastrointestinal blood flow
 - absorption and, 28
 - Gastrointestinal tract, 27, 27. *See also* particular structures
 - absorption from. *See* Absorption
 - drug stability and hydrolysis in, 54-55
 - pH of
 - drug absorption and, 28-29, 40-41, 41t
 - microclimates of, 45
 - physiology of
 - drug absorption and, 27-32
 - Gel(s)
 - aqueous
 - topical application of, to eye, 99-100
 - Gender
 - pharmacokinetic variability due to, 252-253
 - Generic product(s)
 - bioequivalence of, 159-160
 - controlled-release
 - bioequivalence of, 161
 - Genetic factor(s)
 - pharmacokinetic variability due to, 255-266
 - Gentamicin
 - dosage for, in children, 241
 - dosage regimen for
 - adjustment of, in renal disease, 277
 - individualization and optimization of, 351-353
 - furosemide interaction with, 314
 - intramuscular injection of, 88-89
 - peak-to-trough concentration ratio for
 - benefit-to-risk ratio and, 125
 - pharmacokinetics of
 - after burn injury, 299
 - in obesity, 238
 - therapeutic concentration range for, 180t
- Glomerular filtration, 203, 203-204
- Glomerular filtration rate
 - age-related changes in, 245, 246
 - during pregnancy, 254
 - measurement of, 204
- Glucose
 - renal clearance of, 204
- β -Glucuronidase
 - intestinal activity of
 - enterohepatic cycling and, 229
- Glucuronide conjugate(s)
 - formation of, 214, 216t
 - regeneration of parent drug from, in renal disease, 279
- Glycine formation, 214, 216t
- Griseofulvin
 - absorption of
 - crystal form and, 54
 - food's effects on, 34
 - model of, 56
 - particle size and, 51, 67
 - dosing interval for, 13
 - hydrophilic carrier mixed with, 52
 - molecular dispersion of, in polyethylene glycol 6000, 67
 - phenobarbital interaction with, 308
- Guanethidine, loading with, 12
- Guanoxan, oxidation of
 - genetic factors and, 260
- Half-life
 - accumulation and, 11
 - alpha, 16-17
 - beta, 16
 - clearance and, 19, 205
 - clinical significance of, 4
 - creatinine clearance and, in renal disease, 275, 275
 - distribution
 - estimation of, 193-194
 - estimation of, in renal disease, 275
 - in obesity, 240
 - of metabolite
 - estimation of, 221
 - parent drug half-life and, 220
 - plasma protein binding and, 200-201
 - in disease, 291-292
 - terminal, in multicompartmental analysis, 16
 - time to reach steady state and, 9
 - tissue binding and, 201
 - variability in
 - correction for, in bioavailability studies, 149-150
 - volume of distribution and, 19
- Haloperidol
 - individualization and optimization of dosage regimen for, 365-366
- Haloperidol decanoate
 - intramuscular injection of
 - prolonged-release formulation for, 137

- Halothane
 hepatotoxicity of, 219
 Hemodialysis, 278
 Henderson-Hasselbalch equation, 40
 Heparin
 infusion pump for, 94
 intravenous infusion vs. intermittent subcutaneous
 treatment with, 81
 refillable implant of, 138
 Hepatic arterial infusion, 82-84
 local toxicity due to, 85
 Hepatic blood flow. *See under* Blood flow
 Hepatic clearance, 155
 Hepatic extraction ratio, 155-156
 Hepatic first-pass effect. *See* Presystemic metabolism
 Hepatitis
 isoniazid-induced, 257-258
 rifampin and, 323
 Hepatitis B vaccine
 response to
 site of injection and, 88
 Heptabarbital sodium
 absorption of, 49
 Heroin
 effects of, on gastric emptying
 absorption of other drugs and, 31
 Hexachlorophene
 topical application of
 systemic absorption after, 109
 Hexobarbital
 concentration-response relationship for, 177
 rifampin interaction with, 322
 stereoselective metabolism of, 222
 age and, 252
 Hyaluronidase
 in subcutaneous injections, 91
 Hydralazine
 acetylation of
 genetic factors and, 259
 digoxin interaction with, 316, 317
 food's effects on absorption of, 34, 35, 308
 metoprolol interaction with, 333
 propranolol interaction with, 332
 Hydrate
 defined, 53
 Hydrochlorothiazide
 absorption of
 food's effects on, 34, 35
 in malabsorptive states, 37
 peak-to-trough concentration ratio for
 benefit-to-risk ratio and, 125
 pharmacokinetics of, in elderly patients, 246-247
 triamterene with
 absorption of, from capsule vs. tablet, 64
 bioequivalence problems with, 165
 Hydrocortisone
 percutaneous absorption of, 106
 after repeated application, 107-108, 108
 rectal administration of, 117
 topical
 bioequivalence problems with, 172
 Hydrolysis, 214, 215
 in gastrointestinal tract, 54-55, 153, 153
 Hydroquinone
 digoxin complexation with, 57
 21-Hydroxylase deficiency
 prevention of congenital adrenal hyperplasia in, 192
 Hydroxyprogesterone caproate
 intramuscular injection of
 prolonged-release formulation for, 137
 Hyoscyamine
 food's effects on absorption of, 34
 Hyperbilirubinemia
 in neonate
 phenobarbital in treatment of, 320
 plasma protein binding of drugs and, 244
 Hypnotic agent(s). *See also* particular drugs
 delayed absorption of, with food, 308
 Hypoalbuminemia
 adverse drug reactions with, 293-294
 Ibuprofen
 in synovial fluid, 197-198
 metabolism of
 stereoselectivity in, 222
 pharmacokinetics of, in obesity, 239
 Imipenem
 enzyme inhibition with, 217
 Imipramine
 binding of
 α_1 -acid glycoprotein concentration and, 196, 196
 intersubject variability in, 197
 fluphenazine decanoate interaction with, 326
 individualization and optimization of dosage
 regimen for, 367-368, 370
 levodopa interaction with, 307
 pharmacokinetics of
 genetic factors and, 264
 in elderly patients, 251
 Imipramine pamoate
 as slow-release form, 50
 Implant(s). *See also under* Infusion pump(s)
 of prolonged-release medication, 137-138
 Indocyanine green (ICG)
 clearance of, as indicator of hepatic drug
 metabolism, 287
 Indomethacin
 biliary excretion of, 210, 210
 individualization and optimization of dosage
 regimen for, 361
 lithium interaction with, 313, 313
 pharmacokinetics of
 age and, 242t, 243
 probenecid interaction with, 317
 prolonged-release formulation of, using elementary
 osmotic pump, 133
 rectal administration of, 115
 Indoprofen
 metabolism of, 222
 Indoxole
 absorption of
 from oil-in-water emulsion, 62
 from polysorbate 80 solution, 62
 Infant(s). *See also* Neonate(s)
 pharmacokinetics in, 240-241
 Influenza
 pharmacokinetic variability due to, 298-299
 Influenza vaccine
 pharmacokinetic variability due to, 298-299
 Infusion pump(s), 81
 external portable, 92, 94
 for insulin, 93-94, 138
 implantable, 92-93, 94-95, 138
 Inhalation
 drug administration by, 95-97
 Inhaler(s)
 breath-actuated, 96-97
 pressurized metered-dose, 95, 96-97

- Insect repellent(s)
systemic absorption of, 109
- Insecticide(s)
drug interactions with, 337-338
- Insulin
azopolymer-coated, 71
duration of action of
 crystallinity and particle size and, 92
infusion pumps for, 93-94, 138
intramuscular infusion of, for brittle diabetes, 94
intramuscular injection of
 site of, 91-92
intranasal application of, 104-105
intrapertoneal administration of, for brittle diabetes, 94
intravenous infusion of, for brittle diabetes, 94
 lente, 92
nasal absorption of, 103
semilente, 92
subcutaneous injection of, 91-94
 sauna treatment's effect on absorption after, 92, 92
 ultralente, 92
- Intact nephron theory, 272-273
- Interferon
 effects of, on hepatic oxidative metabolism, 298-299
- Interleukin-2 (IL-2)
 intravenous infusion vs. bolus injection of, 81-82
- Intestinal flora
 digoxin metabolism by, 153-154, 214, 308
 age and, 244
 drug metabolism by, 153-154, 214, 229, 229-230
- Intestinal motility
 bioavailability of slowly dissolving drugs and, 51
 changes in, during pregnancy, 254
 drug absorption and, 31-32
- Intestinal resection
 drug absorption and, 37
- Intestinal transit time, 31-32
 prolonged-release medication and, 134
- Intestine(s). *See also* Large intestine
 absorption in, 27-28
 drug metabolism in lumen of, 54-55, 153-154, 229, 229-230. *See also* Intestinal flora
 age and, 244
 drug metabolism in wall of, 157-158, 228-229. *See also* Presystemic metabolism
- Intra-arterial administration, 82-85
 focal toxicity due to, 84-85
- Intramuscular injection, 87-91
 absorption after
 injection site and, 87, 87-89, 89t
 patient-to-patient variability in, 7
 sex differences in, 89, 89t
 bioavailability after, 171
 clearance after, 19
 needle size for, 88, 89-90
 precipitation of drug at injection site after, 90
 prolonged-release, 135-137
- Intranasal application, 102-105
 molecular weight and, 103
- Intrapertoneal administration, 86-87
 for insulin in brittle diabetes, 94
 with implantable infusion pump, 94-95
- Intrathecal administration, 85
- Intrauterine device(s), 139
- Intravaginal application, 101-102
- Intravenous infusion, 81-82
 advantages of, over intermittent treatment, 81
 bolus. *See* Intravenous injection
 clearance after, 19
 dosing schemes for, 81
 extravasation and phlebitis with, 82
 long-term constant rate
 clearance after, 19
 concentration-time profile after, 9, 10
 plasma concentration after
 patient-to-patient variability in, 7
 rate calculation for, 9
 short-term constant rate
 apparent volume of distribution estimation after, 19
 mean residence time after, 20
 plasma concentration after, 4-5, 5
 time course of effect of, 184-185, 185
- Intravenous injection, 80-82
 apparent volume of distribution estimation after, 19
 central access for, 80-81
 of prodrugs
 bioavailability of, 171
 plasma concentration after, 3-4, 4
 time course of effect of, 185, 185-186
- Inulin
 renal clearance of, 204
- Ion exchange resin(s). *See also* Cholestyramine
 drug adsorption by, 58, 307, 317
- Ionization
 drug absorption and, 43-44
 gastrointestinal pH and, 40-41
- Iron
 prolonged-release formulation of, 131
 tetracycline interaction with, 306
- Isoetharine
 intestinal metabolism of, 229
- Isoniazid
 acetylation of
 genetic factors in, 256-258, 257
 enzyme inhibition by
 drug interactions due to, 325-326
 liver damage due to, 257-258, 323
 rifampin interaction with, 323
- Isoproterenol
 gut wall metabolism of, 158, 228
 inhalation of, 96
- Isosorbide dinitrate
 food's effects on absorption of, 33
 sublingual administration of, 113, 114
 tolerance to, 182
- Isosorbide mononitrate
 food's effects on absorption of, 33
- Isotretinoin
 food's effects on absorption of, 34-35
 placental transfer of, 191-192
- Jaundice
 neonatal
 phenobarbital in management of, 320
- Kaolin
 drug adsorption by, 307
- Kaolin-pectin
 drug adsorption by, 58, 307
- Ketamine
 continuous vs. intermittent infusion of, 126
- Ketoconazole
 dissolution and absorption of
 pH and, 47
 enzyme inhibition by, 331

- Ketoprofen
 metabolism of
 stereoselectivity in, 222
 methotrexate interaction with, 313
 pharmacokinetics of, in elderly patients, 252
- Kidney(s)
 disease of. *See* Renal disease
 function of. *See* Renal function
- Labetalol
 enzyme inhibition by
 drug interactions due to, 326
 metabolism of
 stereoselectivity in, 223-224
 pharmacokinetics of
 age and, 249
 time-dependent, 227-228
- Lanoxin (digoxin), 163-164. *See also* Digoxin
- Large intestine
 drug absorption in, 28
 drug delivery to
 acid-resistant coatings for, 71
 drug metabolism in, 229, 229
- Lasix (furosemide), 164-165. *See also* Furosemide
- Leuprolide
 intranasal application of, 104
- Levobunolol
 topical application of, to eye, 101
- Levodopa, 218
 amino acid interaction with, 188-189, 337
 anticholinergic agents' interaction with, 307
 carbidopa with, 217
 central nervous system penetration by, 188-189
 for congestive heart failure, 43
 intestinal transport of, 26
 intravenous infusion vs. intermittent oral treatment
 with, 81
- Levonorgestrel
 subdermal silastic implant of, 138
- Levothyroid (levothyroxine), 165, 166
- Levothyroxine
 bioequivalence problems with, 165, 166
- Lichen sclerosus
 topical testosterone for, 110
- Lidocaine
 cimetidine interaction with, 328, 332
 clearance of
 hepatic blood flow and, 284, 285
 individualization and optimization of dosage
 regimen for, 348-350, 349t, 350
 intramuscular injection of, 87, 87-88
 pharmacokinetics of
 in cardiovascular disease, 294-295, 295
 in liver disease, 286
 time-dependent, 228
 plasma protein binding of, in disease, 290
 propranolol interaction with, 326, 331, 331-332
 rectal administration of, 118
 therapeutic concentration range for, 180t
- Lincomycin
 central nervous system penetration of, 188
 food's effects on absorption of, 33, 308
 kaolin interaction with, 58, 307
 rectal administration of, 114-115
- Lindane
 antipyrine half-life and, 337-338
 topical application of
 systemic absorption after, 109
- Lingua nigra
 salivary excretion of antibiotics and, 211
- Lipid solubility
 drug absorption and, 41-43, 42t
- Lithium
 anti-inflammatory drugs' interaction with, 313, 313
 individualization and optimization of dosage
 regimen for, 366, 366t
 prolonged-release formulation of
 side effects and, 131-132
 salivary excretion of, 211
 tubular reabsorption of, 209
- Lithium carbonate
 prolonged-release formulation of, 130, 130-131
- Lithium sulfate
 food's effects on absorption of, 35
- Liver
 blood flow to. *See under* Blood flow
 disease of. *See* Liver disease
 function of
 antipyrine clearance as measure of, 282, 282t
 involvement of, in metastatic cancer
 intra-arterial drug administration for, 82-84
 isoniazid-induced injury to, 257-258
 rifampin and, 323
 presystemic metabolism in, 154-156. *See also*
 Presystemic metabolism
 time-dependent, 227-228
 volume of, in elderly patient, 247
- Liver disease
 albumin binding of drugs in, 289-290
 pharmacokinetic variability due to, 280-288
 clinical significance of, 287-288
 prediction of, 286-287
- Loading dose, 12
 adjustment in, for patients with impaired drug
 binding, 292
 estimation of, 9, 12
 necessity for, in renal disease, 276
- Lorazepam
 binding of
 intersubject variability in, 197
 clearance of, as indicator of hepatic drug
 metabolism, 287
 pharmacokinetics of
 age and, 248
 gender differences in, 253
 in liver disease, 283
 in obesity, 240
 in renal disease, 279
 sublingual administration of, 112
- Lubricant(s)
 in tablets
 dissolution and, 66
- Lung(s)
 drug absorption from, 95
 drug metabolism in, 193, 230
- Lung cancer
 debrisoquin oxidation phenotype and, 261-262
- Lupus-like syndrome
 with hydralazine therapy
 acetylation phenotype and, 259
 with procainamide therapy
 acetylation phenotype and, 258-259, 259
- Luteinizing hormone-releasing hormone agonist(s)
 intramuscular injection of
 prolonged-release formulation for, 136
 intranasal application of, 104
- Macrochantin (nitrofurantoin), 166-167. *See also*
 Nitrofurantoin

- Malabsorption**
 defined, 36
 drug absorption and, 36-37
 drug-induced, 36
- Mannitol**
 blood-brain barrier disruption by, 189-190
- Maprotiline**, 366-367
- Maxzide (hydrochlorothiazide/triamterene)**, 165. *See also under Hydrochlorothiazide*
- Mean absorption time (MAT)**
 in absorption rate estimation, 152, 153
- Mean dissolution time (MDT)**, 152, 153
- Mean residence time (MRT)**, 18, 19-20
 of metabolite
 calculation of, 221
- Medroxyprogesterone acetate (MPA)**
 absorption of
 particle size and, 51
 intramuscular injection of
 prolonged-release formulation for, 137
- Membrane physiology**, 24-27
- Meningitis**
 permeability of blood-brain barrier in, 188
- Meperidine**
 effects of, on gastric emptying
 absorption of other drugs and, 31
 metabolites of, 214
 accumulation of, in renal disease, 279t
 pharmacokinetics of, 192-193
 age and, 242t
 in liver disease, 285
 phenytoin interaction with, 319
 saliva/plasma concentration ratio for, 212
- Mephénytoin**
 polymorphic hydroxylation of, 265-266
- Mephobarbital**
 metabolism of
 genetic factors and, 266
- Meprobamate**
 alcohol interaction with, 334
 pharmacokinetics of, in cholestasis, 286
- Meptazinol**
 rectal administration of, 118
- Mercaptopurine**
 allopurinol interaction with, 323-324
- Mesalamine**. *See* 5-Aminosalicylic acid
- Metabolism**, 213-230
 capacity-limited, 224-226
 concentration-dependent, 224-226
 defined, 213-214
 dose-dependent, 226-227
 drug interactions involving, 317-334
 extrahepatic, 228-230
 hepatic
 antipyrine kinetics as indicator of, 281, 281-282, 282t
 in children, 245
 in intestinal lumen, 54-55, 153-154, 229, 229-230. *See also under Intestinal flora*
 age and, 244
 in newborns, 242t, 242-244
 in renal disease, 279-280
 in thyroid disease, 298
 induction and inhibition of enzymes involved in. *See*
 Enzyme induction; Enzyme inhibition
 nonlinear, 224-228
 pathways of, 214, 215t-216t
 plasma protein binding and, 200
 presystemic. *See* Presystemic metabolism
 species differences in, 221, 221t
 stereoselective, 221-224
 age and, 252
- Metabolite(s)**
 active, 218-220
 concentration-response relationships and, 181
 disposition of, 220
 fraction of parent drug converted to
 estimation of, 220-221
 kinetics of, 220-221
 FDA requirements for determination of, for
 generic products, 159
 renal disease's effects on, 279t, 279-280
- Methacycline**
 ferrous sulfate interaction with, 306
- Methicillin**
 gastric degradation of, 54
- Methimazole**
 pharmacokinetics of
 in pregnancy, 255
 in thyroid disease, 298
- Methotrexate**
 continuous vs. intermittent administration of, 125
 crystalluria due to, 209
 individualization and optimization of dosage
 regimen for, 363-364
 ketoprofen interaction with, 313
 probenecid interaction with, 209, 311
 renal clearance of
 urine pH and, 208
- Methoxsalen**
 enzyme inhibition by, 331
- Methoxyflurane**
 renal toxicity of, 219
- Methylcellulose**
 in nitrofurantoin suspension
 absorption and, 63
 tablet coating with, 67
 treatment of poorly water-soluble drugs with
 absorption from capsules and, 64
- Methyldopa**
 intestinal transport of, 26
- Methylphenidate**
 metabolism of
 stereoselectivity in, 223
- Methylprednisolone**
 rectal administration of, 117, 117
- Methylprednisolone acetate**
 intramuscular injection of
 prolonged-release formulation for, 136
- Methyltestosterone**
 sublingual administration of, 113
- Methylxanthine(s)**. *See also* particular drugs
 individualization and optimization of dosage
 regimens for, 370-371
- Metoclopramide**
 effects of, on gastric emptying
 absorption of other drugs and, 31, 32
 effects of, on intestinal transit time
 absorption of other drugs and, 32
 individualization and optimization of dosage
 regimen for, 364
 intravenous infusion vs. intermittent treatment with,
 81
- Metoprolol**
 enzyme inhibition by
 drug interactions due to, 326
 food's effects on absorption of, 35
 hydralazine interaction with, 333
 oral contraceptives' interaction with, 327

- Metoprolol (*cont'd.*)
 pharmacokinetics of
 age and, 249
 genetic factors and, 262
 in liver disease, 285
 in pregnancy, 255
 prolonged-release formulation of, 127, 128
 using elementary osmotic pump, 132-133, 133
 propafenone interaction with, 331
 rifampin interaction with, 322
 salivary excretion of, 211
- Metronidazole
 intravaginal application of, 102
 rectal administration of, 117
 warfarin interaction with, 325
- Michaelis-Menten equation, 224
- Michaelis-Menten kinetics, 224-226
 defined, 226
- Micronization
 aggregation after
 strategies for reducing, 52
 dissolution and, 51-52
- Midazolam
 pharmacokinetic variability of, 235
 pharmacokinetics of
 age and, 248
 presystemic metabolism of, 157
- Migraine, gastric emptying and, 30-31
- Milk, drug excretion in, 212-213
- Minoxidil
 topical application of
 systemic absorption after, 109
- Mitomycin
 hepatic arterial injection of, with starch
 microspheres, 84
- Molecular weight
 biliary excretion and, 210, 210
 intranasal absorption and, 103
- Moment analysis, 17-21
 absorption rate estimation using, 152-153
- Monosaccharide(s)
 intestinal transport of, 26
- Morphine
 buccal administration of, 111
 prolonged-release formulation for, 142
 epidural administration of, 85-86
 continuous on-demand, 86
 intrathecal, 85
 metabolism of, 218
 intestinal, 229
 pharmacokinetics of
 age and, 243
 in renal disease, 279
 rectal administration of, 114
- Morphine-6-glucuronide (M6G), 218
- Moxalactam
 dosage regimen for
 adjustment of, in renal disease, 275-276
- Mucin
 drug complexation with, 57
- Mucosal unstirred layer, 44
 drug absorption and, 44-45
 gastric
 protective role of, 44-45
- N-acetylcysteine
 for nitrate tolerance, 183
- Nadolol
 renal clearance of, in renal disease, 273t, 273, 273
- Nafarelin
 intranasal application of, 104
- Naproxen
 pharmacokinetics of, in elderly patients, 251-252
 rectal administration of, 115
- Naproxen sodium
 absorption of, 49
- Nasal administration, 102-105
 molecular weight and, 103
- Nasolacrimal occlusion
 to prevent systemic absorption of ophthalmic
 medications, 101
- Nebulizer(s), 97
- Neomycin
 digoxin interaction with, 308
- Neonate(s)
 pharmacokinetics in, 240-241, 242t, 242-244
 plasma protein binding in, 244, 244t
 renal excretion in, 245
- Neuroleptic(s). *See also* particular drugs
 dosing interval for, 13
 enzyme inhibition by
 drug interactions due to, 326
 individualization and optimization of dosage
 regimens for, 365-366
- Newborn(s). *See* Neonate(s)
- Nicardipine
 concentration-dependent elimination of, 226
- Nicotine
 distribution of, 193
 tolerance to, 183
 distribution kinetics vs., 193
- Nicotine gum, 111-112
- Nicoumalone
 cimetidine interaction with, 328
 metabolism of
 stereoselectivity in, 223
- Nifedipine
 cimetidine interaction with, 329
 food's effects on absorption of, 34
 pharmacokinetics of
 age and, 250
 in liver disease, 285
 sublingual administration of, 113
- Nimodipine
 pharmacokinetics of, in liver disease, 286
- Nitrate(s). *See also* particular drugs
 tolerance to, 182-183
- Nitrazepam
 pharmacokinetics of, in obesity, 239-240
- Nitrendipine
 pharmacokinetics of, in liver disease, 286
- Nitrofurantoin
 absorption of
 food's effects on, 35, 35t
 in suspension with methylcellulose, 63
 bioequivalence problems with, 166-167
 dissolution of
 bioavailability and, 76-77
- Nitrogen mustard
 serine and threonine derivatives of
 intestinal transport of, 26
- Nitroglycerin
 intranasal application of, 102
 nonlinear metabolism of, 226-227
 oral aerosol spray of, 112
 sublingual administration of, 111
 tolerance to, 182-183
 topical, 110
 with intravenous infusion, 82

- transdermal, 140-141
 tolerance problems with, 182-183
 transmucosal controlled-release formulation of, 142
- Nitroprusside
 digoxin interaction with, 316, 317t
 intravenous infusion of
 time course of effect of, 185, 185
- Nizatidine
 renal excretion of, 276
- Nonsteroidal anti-inflammatory drug(s). *See also*
 particular drugs
 effects of, on renal function
 drug interactions due to, 313, 313
 individualization and optimization of dosage
 regimens for, 359-361
 metabolism of
 stereoselectivity in, 222-223
 pharmacokinetics of, in elderly patients, 251-252
- Nordiazepam (desmethyldiazepam)
 cimetidine interaction with, 328, 328t
 clearance of, in obesity, 239
 prodrug of, 50, 54, 218
- Norethindrone
 brain-selective delivery of, 190
- Norethindrone enanthate
 intramuscular injection of
 prolonged-release formulation for, 137
- Norfloracin
 antacid interaction with, 307
 sucralate interaction with, 307
 theophylline interaction with, 330
- Normeperidine, 218
- Nortriptyline
 in cerebrospinal fluid, 197
 individualization and optimization of dosage
 regimen for, 367, 367t, 369, 369-370
 pharmacokinetic variability of, 235-236
 pharmacokinetics of
 age and, 242t
 genetic factors and, 260, 260
 in elderly patients, 251
 plasma protein binding of, 197
 presystemic metabolism of, 156, 157
 therapeutic concentration range for, 180t
- Novobiocin
 absorption of
 crystal form and, 53
 bioavailability of salts of, 49
- Noyes-Whitney equation, 46
- Obesity
 pharmacokinetic variability due to, 237-240
- Occlusive dressing(s)
 percutaneous drug absorption and, 106
- Ocular administration. *See under* Eye
- Ocusert, 138-139, 139
- Oil
 drugs dissolved in, 62
- Oil-in-water emulsion(s)
 drugs dissolved in, 62
 drugs suspended in, 63
- Omeprazole
 enzyme inhibition by
 drug interactions due to, 331
- Ophthalmic medication. *See* Eye
- Opiate(s). *See also* particular drugs
 spinal administration of, 85-86
- Opioid analgesic(s). *See also* particular drugs
 continuous subcutaneous infusion of, with portable
 pump, 95
- Oral administration
 absorption after. *See* Absorption
 clearance after, 19
 plasma concentration after
 patient-to-patient variability in, 7
 prolonged-release formulations for. *See under*
 Prolonged-release medication
 repetitive
 plasma concentration after, 10-11, 11
- Ordered mixture, 52
- Orosomucoid. *See* α_1 -Acid glycoprotein
- Osmotic pump, 132-133, 132-134
 rectal administration using, 142-143
 subcutaneous implantation of, 138
- Osteomyelitis
 implantable infusion system for amikacin for, 94, 138
- Oxazepam
 binding of
 intersubject variability in, 197
 dissolution of
 bioavailability and, 76, 77
 pharmacokinetics of
 age and, 248
 gender differences in, 253
 in liver disease, 283
 in obesity, 240
 in thyroid disease, 297, 298
- Oxidation, 214, 215t
 polymorphic
 debrisoquin type, 260-265
 mephenytoin type, 265-266
- Oxprenolol
 enzyme inhibition by
 drug interactions due to, 326
 pharmacokinetics of
 age and, 249
- Oxymorphone
 rectal administration of, 115
- Oxypurinol. *See also* Allopurinol
 accumulation of, in renal disease, 279t
- Oxytetracycline
 bioequivalence problems with, 167, 167
 ferrous sulfate interaction with, 306
- Oxytetracycline dihydrate
 bioequivalence problems with, 167, 167
- Oxytetracycline hydrochloride
 bioequivalence problems with, 167
- Oxytocin
 intranasal application of, 103-104
- Pain
 gastric emptying and, 30-31
- Pancuronium
 pharmacokinetics of, in cholestasis, 286
- Papaverine
 bioequivalence problems with, 167
- Para-aminohippuric acid (PAH)
 renal clearance of, 204
- Para-aminosalicylic acid (PAS)
 bioequivalence problems with, 161
- Parkinson's disease
 diet-drug interactions in, 188-189, 337
- Particle size
 dissolution and, 51-53
- Pectin
 kaolin with
 drug adsorption by, 58, 307

- Pefloxacin
theophylline interaction with, 330
- Penetration enhancer(s)
for topical formulations, 107
- Penicillamine
food's effects on absorption of, 33
intestinal transport of, 26
- Penicillin(s). *See also* particular drugs
food's effects on absorption of, 33
probenecid interaction with, 311
- Penicillin G
central nervous system penetration of, 188
competitive inhibition of tubular secretion of, 206
gastric degradation of, 52, 54
intramuscular injection of
prolonged-release formulation for, 136
rectal administration of, 114
renal clearance of, 204
- Penicillin V
bioavailability of salts of, 49
- Penitamide
aerosolized, 96
- Pentazocine
pharmacokinetics of
in liver disease, 285
in smokers, 335
presystemic metabolism of, 156, 156
- Pentobarbital
absorption of
dosage form and, 61
alcohol interaction with, 334
alprenolol interaction with, 321
intramuscular injection of, 89, 90
pharmacokinetics of, in cholestasis, 286
- Peptide(s)
azopolymer-coated, 71
intranasal application of, 102
- Percutaneous absorption
after repeated application, 107-108, 108
dose-response relationships in, 107, 108t
drug factors affecting, 106-107
estimation of, 108
skin factors affecting, 106
systemic, 109-110
- Perhexiline
adverse effects of
debrisoquin oxidation status and, 260
- Personality
debrisoquin oxidation phenotype and, 262
- pH
dissolution and, 46-48
gastrointestinal. *See under* Gastrointestinal tract
urine. *See* Urine pH
- Pharmacodynamic variability
defined, 176
- Pharmacogenetics, 256
- Pharmacokinetic variability, 176-177, 234-343
age and, 242t, 242-252
defined, 176
disease and, 272-304
drug interactions and, 305-343
gender and, 252-253
genetic factors and, 255-266
intersubject vs. intrasubject, 235
pregnancy and, 253-255
- Pharmacokinetics
clinical
defined, 1
concentration-dependent, 224-226
defined, 226
defined, 1
dose-dependent, 226-227
first-order, 3-4, 4
introduction to, 1-13
linear
dose proportionality and, 2
multicompartmental, 14-15, 14-17
problems with, 17
noncompartmental, 17-23
time-dependent, 227, 227-228
variability in. *See* Pharmacokinetic variability
- Phenacetin
absorption of
particle size and, 52, 52t
metabolites of, 214-216
pharmacokinetics of
diet's effects on, 336
genetic factors and, 260
in smokers, 335, 335t
presystemic metabolism of, 157-158
- Phenindione
cimetidine interaction with, 328
variable effect of, 234
- Phenobarbital
binding of, during pregnancy, 254
cerebrospinal fluid-plasma concentration ratio for, 189
dissolution of
pH-dependent, 47
rate of, 49t
distribution half-life of, 194
distribution of
plasma pH and, 188
elimination of
charcoal's effect on, 211
enzyme induction by
drug interactions due to, 319, 320
griseofulvin interaction with, 308
hypersensitivity to, 219
individualization and optimization of dosage
regimen for, 355
pharmacokinetics of
age and, 244t
during pregnancy, 255
polyethylene glycol 4000 complexation with, 57
saliva/plasma concentration ratio for, 212
therapeutic concentration range for
seizure type and, 358
valproic acid interaction with, 327
- Phenobarbital sodium
absorption of, 49
dissolution rate of, 49t
- Phenothiazine(s). *See also* particular drugs
enzyme inhibition by
drug interactions due to, 326
- Phenprocoumon
allopurinol interaction with, 324
cholestyramine interaction with, 58, 317
gender differences in metabolism of, in rats, 253
individualization and optimization of dosage
regimen for, 364
propafenone interaction with, 331
- Phenylbutazone
bioequivalence problems with, 167-168
chlorinated pesticides' interaction with, 338
elimination of
charcoal's effect on, 211
enzyme inhibition by
drug interactions due to, 324
pharmacokinetics of

- age and, 242t
twin studies of, 256, 256t
plasma protein binding of
 drugs interfering with, 309
 in liver disease, 289-290
- Phenylephrine**
 topical application of, to eye
 systemic absorption after, 100
- Phenylephrine hydrochloride**
 ophthalmic
 variable effect of, 234
- Phenytoin**
 absorption of
 from aqueous suspension, 63, 63
 in malabsorptive states, 36-37
 adverse reactions to
 serum albumin and, 293
 binding of
 drugs interfering with, 309
 during pregnancy, 254
 in renal disease, 181, 288, 289
 intersubject variability in, 197
 bioequivalence problems with, 168, 168t
 carbamazepine interaction with, 321
 cerebrospinal fluid-plasma concentration ratio for,
 189
 chloramphenicol interaction with, 323, 323
 cimetidine interaction with, 328, 329
 disulfiram interaction with, 323
 dosing interval for, 13
 enzyme induction by, 318
 drug interactions due to, 319-320
 excretion of, in milk, 212-213
 hypersensitivity to, 219
 individualization and optimization of dosage
 regimen for, 355-358, 356t, 357
 intramuscular injection of, 90, 91
 bioavailability after, 171
 intravenous injection of, 80
 isoniazid interaction with, 257, 325
 loading with, 12
 metabolites of, 214
 methylcellulose treatment of
 absorption from capsules and, 64
 omeprazole interaction with, 331
 pharmacokinetic variability of, 235, 235
 pharmacokinetics of
 age and, 242t, 243, 244t
 concentration-dependent, 224, 225, 225
 in elderly patient, 247
 in pregnancy, 255
 in renal disease, 291
 placental transfer of, 191, 191t
 plasma concentration of
 free, drug effects and, 199
 in renal disease, 288, 288, 292-293, 294
 prodrug of, 50
 renal clearance of, 204
 rifampin interaction with, 322
 salivary excretion of, 211
 sucralfate interaction with, 307
 therapeutic concentration range for, 180t, 181
 in patients with impaired drug binding, 293
 seizure type and, 358
 thioridazine interaction with, 326
 valproic acid interaction with, 310
- Phenytoin sulfate**
 solubility of, 50
- Phlebitis**
 with intravenous infusion, 82
- pH-partition theory, 40-43
 deviations from, 43, 43-45
- Pilocarpine**
 topical application of, to eye, 98, 99
 dosage form and, 100, 100
 prolonged-release ocular insert for, 126, 138-139,
 139
- Pindolol**
 stereoselective renal clearance of, 207
- Pituitary hormone(s)**
 intranasal application of, 104
- Pivampicillin**, 42
- Placenta**
 drug transfer across, 190-192, 191
- Plasma concentration**
 after extravascular administration, 5-6, 6
 after intramuscular administration
 patient-to-patient variability in, 7
 after intravenous administration
 patient-to-patient variability in, 7
 after intravenous injection, 3-4, 4
 after long-term constant rate infusion, 9, 10
 after oral administration
 patient-to-patient variability in, 7
 repetitive, 10-11, 11
 after short-term constant rate intravenous infusion,
 4-5, 5
 at steady state. *See under* Steady state
 clinical response and, 176-186
 free. *See also* Binding
 drug effects and, 199
 in patients with impaired drug binding, 292
 parameters based on, 22-23
 total vs., 180-181, 196-197
 measurement of
 in optimization of dosage regimens, 345-347
- peak**
 after extravascular administration, 5-6
 after intravenous infusion vs. bolus injection, 5,
 16-17
 gastric emptying and, 29, 30, 30
 pharmacokinetic considerations of, 3, 3-7
 physical significance of, 2
 therapeutic effectiveness and, 179, 179-180
 therapeutic range for, 180, 180t, 346
 time course of. *See* Concentration-time profile
- Plasma volume**
 determination of, 194
- Pneumocystis carinii* pneumonia**
 aerosolized pentamidine for, 96
- Polyethylene glycol 400**
 effects of, on absorption, 62
- Polyethylene glycol 4000**
 phenobarbital complexation with, 57
- Polymorphism**, 53
- Polyneuritis**
 with isoniazid therapy, 257
- Polyorbate 80**
 effects of
 on absorption, 62
 on dissolution, 52, 52t
- Polyvinylpyrrolidone (PVP)**
 absorption of, in malabsorptive states, 36
- Posture**
 drug absorption and, 30, 30
 theophylline absorption and, 129-130
- Potassium chloride**
 enteric-coated
 toxicity due to, 70-71

- Practolol
furosemide interaction with, 314
- Prazosin
pharmacokinetics of, in cardiovascular disease, 296
- Precipitation
at intramuscular injection site, 90
of drugs in solution, 62
- Prednisolone
bioavailability of, after intravenous injection of prodrug, 171
enteric-coated
absorption of, 68, 69t
oral contraceptives' interaction with, 327
phenytoin interaction with, 319
rectal administration of, 117
- Prednisolone acetate
intramuscular injection of
prolonged-release formulation for, 136
topical application of, to eye, 99-100
- Prednisolone phosphate
intravenous injection of
prednisolone bioavailability after, 82, 171
- Prednisolone phthalate
intravenous injection of
prednisolone bioavailability after, 82, 171
- Prednisolone sodium phosphate
topical application of, to eye, 99-100
- Prednisolone sodium succinate
intravenous administration of, 82
- Prednisone, 218
adverse reactions to
serum albumin and, 293
dissolution of
bioavailability and, 77, 77
- Pregnancy
pharmacokinetic variability due to, 253-255
placental drug transfer during, 190-192, 191
- Press-coated tablet(s), 67-68
- Presystemic metabolism, 28, 154-158, 155
age-related changes in, 247
enzyme induction's effects on, 318-319
gut wall, 157-158, 228-229
hepatic, 154-156
time-dependent, 227-228
pharmacokinetic variability and, 235-236
renal disease's effects on, 279-280
- Primidone
active metabolite of, 218
generic
bioequivalence problems with, 159-160
individualization and optimization of dosage regimen for, 355
phenytoin interaction with, 319
- Probenecid
competitive inhibition of biliary secretion by, 209
competitive inhibition of tubular secretion by, 206, 311
drug interactions with, 311-312
indomethacin interaction with, 317
methotrexate interaction with, 209, 311
penicillin interaction with, 206, 311
- Procainamide
acetylation of
genetic factors and, 258-259, 259
active metabolite of, 218
accumulation of, in renal disease, 279t
bioequivalence problems with, 168-169
cimetidine interaction with, 312-313
dosage regimen for
adjustment of, in renal disease, 275
individualization and optimization of, 347
pharmacokinetics of
age and, 245
plasma concentration of
therapeutic effectiveness and, 179, 179-180
prolonged-release formulation of, 131, 132
saliva/plasma concentration ratio for, 211
therapeutic concentration range for, 180t, 180
uptake of, in ischemic and nonischemic myocardium, 192, 192
- Procaine penicillin G
intramuscular injection of
prolonged-release formulation for, 136
- Procan-SR (procainamide), 168-169. *See also* Procainamide
- Prodrug(s), 42, 218
failure of conversion of, 54-55
toxicity due to, 55
for drug delivery to central nervous system, 190
hydrolysis of, in gastrointestinal fluids, 54-55
intravenous administration of, 82
bioavailability after, 171
lipid soluble, 42-43
water soluble, 50-51
- Product inhibition, 226
time-dependent kinetics due to, 227
- Progesterone, 139
- Progesterone
in intrauterine device, 139
- Prolonged-release medication, 124-145
advantages of, 125-126
bioavailability of
regulatory and clinical considerations involving, 160-161
buccal, 142
defined, 124
intrauterine, 139
ocular, 138-139
oral, 126-135
criteria for evaluation of, 126
for zero-order release, 132-133, 132-134
limitations of, 134-135
single-unit, 127
steady-state fluctuations and elimination rate for, 131
subdivided, 127
techniques for development of, 126-127
variability in performance of, 127-128
parenteral, 135-138
pharmacokinetic theory applied to, 124-126
rectal, 142-143
transdermal, 139-142
- Promazine
attapulgitic or charcoal adsorption of
absorption and, 57-58
kaolin interaction with, 307
- Pronestyl-SR (procainamide), 168-169. *See also* Procainamide
- Propafenone
enzyme inhibition by
drug interactions due to, 331
pharmacokinetics of
concentration-dependent, 226
genetic factors and, 263-264
- Propanteline
effects of, on gastric emptying, 29
absorption of other drugs and, 31, 32
effects of, on intestinal transit time
absorption of other drugs and, 32
food's effects on, 34, 308
- Propoxyphene

- efficacy of, in smokers, 334
 enzyme inhibition by
 drug interactions due to, 330
 metabolite of
 accumulation of, in renal disease, 279t
Propranolol
 absorption of
 food's effects on, 35-36, 36
 in malabsorptive states, 37
 in thyroid disease, 297
 apparent volume of distribution of, in disease, 291
 chlorpromazine interaction with, 325, 326
 cholestyramine adsorption of, 58
 cimetidine interaction with, 332
 clearance of
 binding and, 291-292
 in liver disease, 291
 colestipol adsorption of, 58
 concentration-effect curves for
 for oral vs. intravenous doses, 181, 181
 enzyme inhibition by
 drug interactions due to, 326
 excretion of, in milk, 212-213
 free concentration of
 drug effects and, 199
 hydralazine interaction with, 332
 intranasal application of, 102
 lidocaine interaction with, 331, 331-332
 metabolism of
 presystemic, 156
 stereoselectivity in, 222
 metabolites of
 elevated levels of, in uremic patients, 220
 pharmacokinetic variability of, 236, 236
 pharmacokinetics of
 age and, 248-249
 concentration-dependent, 226
 genetic factors and, 262, 266
 in cardiovascular disease, 295
 in liver disease, 285
 in obesity, 239
 in renal disease, 279-280
 in thyroid disease, 297, 298
 time-dependent, 227
 plasma protein binding of, in disease, 290
 prolonged-release formulation of, 127
 rectal administration of, 118
Propylene glycol
 as solvent for intramuscular injections, 91
Propylthiouracil
 elimination of, in thyroid disease, 298
Pseudoephedrine
 renal clearance of
 urine flow rate and, 209
 urine pH and, 208
Psychotropic drug(s). *See also* particular drugs and classes of drugs
 individualization and optimization of dosage regimens for, 365-370
Pulmonary extraction ratio, 193
Pyrvinium pamoate
 absorption of
 particle size and, 51

 as probe of metabolic pathways regulated by
 debrisoquin phenotype, 333-334
 binding of
 in disease, 290
 to erythrocytes, 198, 198
 bioequivalence problems with, 169, 169
 cimetidine interaction with, 328
 concentration-response relationship for, for oral vs.
 intravenous doses, 181
 digoxin interaction with, 314-315, 314-316
 individualization and optimization of dosage
 regimen for, 347-348
 pharmacokinetics of
 age and, 245
 in cardiovascular disease, 295-296
 rifampin interaction with, 322, 322
Quinolone antibiotic(s)
 absorption of
 drugs interfering with, 307
 enzyme inhibition by
 drug interactions due to, 330

Rabies vaccine
 intramuscular injection of, 88
Racemate(s)
 concentration-response relationship for, 181
 metabolism of, 222-224
 age-related changes in, 252
 nonstereoselective assay of
 problems with, 224
 tubular secretion of, 206-207
Radiation therapy
 gastrointestinal damage due to
 digoxin absorption after, 36
Ranitidine
 cimetidine interaction with, 313
 pharmacokinetics of, in elderly patients, 246
 renal excretion of, 276
Rate constant. *See also* Absorption rate constant;
 Elimination rate constant
 defined, 3
 for first-order portion of concentration-time profile,
 15
Rectal Administration, 113-118
 bioavailability after, 171
 prolonged-release medication for, 142-143
Redistribution
 duration of effect and, 192
Reduction, 214, 215t
Renal blood flow
 drug-induced changes in
 interactions due to, 316
Renal clearance, 204-206
 free plasma concentration and, 200, 205-206
Renal disease
 albumin binding of drugs in, 288-289, 288-289
 dosage regimen adjustments in, 275-277
 pharmacokinetic variability due to, 272-280
Renal excretion, 203-209
 drug interactions involving, 310-316
 in newborns, 245
 in renal disease, 273, 273, 273t
 in thyroid disease, 297-298
 of metabolites, 220
 physiology of, 203, 203-204
Renal function
 assessment of, 272
 in elderly patient, 247
 serum creatinine for, 278-279

- Renal plasma flow rate
measurement of, 204
- Response
all-or-none (quantal)
model of concentration-response relationship with,
178, 178-179
time course of, 183-184
delays in
concentration-response relationship and, 181, 181-
182
graded
quantitative models of, 177-178, 177-178
time course of, 184-186
plasma concentration and, 176-186
plasma protein binding and, 199
time course of. *See* Duration of effect
- Retinoic acid. *See* Isotretinoin
- Retinoic acid embryopathy, 191
- Rh-incompatibility
phenobarbital in management of, 320
- Riboflavin
absorption of
food's effects on, 34, 34t
in thyroid disease, 297
bioavailability of
dose and, 26-27, 27
intestinal motility and, 32
tubular reabsorption of, 209
- Rifampin
biliary excretion of, 210
enzyme induction by
drug interactions due to, 321-322, 322-323
food's effects on absorption of, 33
pharmacokinetics of, in cholestasis, 286
salivary excretion of, 211
- Rimiterol
intestinal metabolism of, 229
- Salbutamol
metabolism of, in gut wall, 158, 229
- Salicylate. *See also* Aspirin
adverse reactions to
urine pH and, 311
antacid interaction with, 311
individualization and optimization of dosage
regimen for, 359-361, 360
metabolites of, 214
pharmacokinetics of
concentration-dependent, 224, 225
in obesity, 240
time-dependent, 227
plasma protein binding of, in liver disease, 289-290
- Salicylic acid
absorption of, 43, 43
dissolution of
pH-dependent, 47
rate of, 49t
pharmacokinetics of
gender differences in, 253
therapeutic concentration range for, 180, 180t
topical application of
systemic absorption after, 109
- Saliva
drug concentration in, 187
monitoring of, 354
excretion in, 211-212
- Salt(s)
dissolution rate of, 48-50, 49t
in situ formation of, 50
- Schizophrenia
prolonged-release intramuscular medication for, 136-
137
- Scopolamine
transdermal, 140
- Secobarbital
rectal administration of, 116
warfarin interaction with, 320
- Secobarbital sodium
absorption of, 49
- Self-induction. *See* Autoinduction
- Semilogarithmic plotting, 3-4, 4
- Shellac
as enteric coating, 68
- Skin
application to, 105-110
absorption after. *See* Percutaneous absorption
bioavailability after, 171-172
site of, 106
drug metabolism in, 228
structure of, 105
- Skin stripping, 106
for estimating percutaneous absorption, 108
- Slow-release medication. *See* Prolonged-release
medication
- Small intestine. *See also* Intestine(s)
drug absorption in, 27-28
enzymatic hydrolysis of drugs in, 153
- Smoking
enzyme induction by, 216, 317
age and, 247, 249
pharmacokinetic variability due to, 334-336, 335t
propranolol pharmacokinetics and, 249
theophylline pharmacokinetics and, 248, 335
- Sodium benzoate
dissolution rate of, 49t
- Sodium bicarbonate
stimulants administered with
detection of, in urine, 208
- Sodium cromoglycate
nasal absorption of, 103
- Solid dosage form(s). *See also* Capsule(s); Tablet(s)
absorption from, 45-54
- Solution(s)
biopharmaceutic characteristics of, (c)
drug absorption from, 40-45
- Solvate(s), 53-54
- Solvent(s)
for intramuscular injections, 91
for intravenous injections, 80
- Spansule, 127
- Sparteine
polymorphic oxidation of, 261
inheritance of, 260
- Spinal administration, 85-86
- Spirinolactone
bioavailability of
particle size and, 51
- Stable isotope studies
of distribution, 193-194
- Starch microsphere(s)
for hepatic blood flow control, 83-84
- Steady state, 9
bioavailability studies at, 149, 150
concentrations at
average, 11-12, 21-22, 21-22
for drugs with concentration-dependent
elimination, 225, 225-226
prediction of, 21-22, 21-22, 379, 379t
with prolonged-release medication, 125-126, 131

- with repetitive oral dosing, 10
- time to reach, 9
- prediction of, 22
- Stereoselectivity
 - in drug interactions, 333
 - in metabolism, 221-224
 - age and, 252
 - in tubular secretion, 206-207
- Steroid(s). *See* Corticosteroid(s); particular drugs
- Stomach
 - chemical degradation of drugs in, 52-53, 153
 - drug absorption in, 27
 - solubility and, 47
 - mucosal unstirred layer of
 - protective role of, 44-45
- Stratum corneum, 105
- Subcutaneous infusion(s)
 - portable pumps for insulin administration, 93-94
- Subcutaneous injection(s), 91-95
- Sublingual administration, 110-113
 - disintegration test for tablets for, 73
- Succinylsulfathiazole
 - absorption of
 - crystal form and, 54
- Sucralfate
 - interference of, with absorption of other drugs, 307
- Sugar-coated tablet(s), 67
- Sulfadiazine
 - acetylation of
 - genetic factors and, 258
 - plasma protein binding of, in liver disease, 289-290
- Sulfadimidine
 - acetylation of
 - genetic factors and, 258
- Sulfaethidole
 - half-life of
 - urine pH and, 207
- Sulfalene
 - elimination of
 - urine pH and, 207-208
- Sulfameter
 - absorption of
 - crystal form and, 53
- Sulfamethazine
 - acetylation of
 - genetic factors and, 258
- Sulfamethizole
 - enzyme inhibition by
 - drug interactions due to, 325
- Sulfamethoxazole
 - renal clearance of
 - urine pH and, 208, 208
 - trimethoprim with
 - warfarin interaction with, 325
- Sulfamethoxypyrazine
 - pharmacokinetics of
 - age and, 244t
- Sulfamethoxypyridazine
 - pharmacokinetics of
 - age and, 242t, 242
- Sulfaphenazole
 - tolbutamide interaction with, 325
- Sulfapyridine. *See also* Sulfasalazine
 - acetylation of
 - genetic factors and, 258
- Sulfasalazine, 71
 - adverse effects of
 - acetylator phenotype and, 258
 - bioavailability of
 - intestinal motility and, 32
 - digoxin interaction with, 308
 - intestinal metabolism of, 229, 229
 - oral antibiotics' effects on, 154
 - rifampin interaction with, 322
- Sulfasymazine
 - renal clearance of
 - diurnal variation in, 208-209
 - urine pH and, 207-208
- Sulfate conjugation, 214, 216t
- Sulfathiazole
 - dissolution rate of, 49t
- Sulfinpyrazone
 - enzyme inhibition by
 - drug interactions due to, 324
- Sulfisoxazole
 - pharmacokinetics of
 - age and, 244t
 - renal clearance of
 - mechanisms of, 207
- Sulfonamide(s). *See also* particular drugs
 - acetylation of
 - genetic factors and, 258
 - crystalluria due to, 209
 - elimination of
 - urine pH and, 207-208, 208
 - enzyme inhibition by
 - drug interactions due to, 325
- Sulindac
 - biliary excretion of, 210
 - intestinal metabolism of, 229-230
 - pharmacokinetics of
 - in liver disease, 283
 - in renal disease, 280
- Superposition
 - method of, 379, 379t
- Surface area. *See* Body surface area
- Surfactant(s)
 - in solution preparation, 62
 - nasal drug absorption and, 103
- Suspension(s)
 - absorption from, 45-54
 - biopharmaceutic characteristics of, 63
 - topical application of, to eye, 99, 99
- Sustained-release medication. *See* Prolonged-release medication
- Synovial fluid
 - drug concentration in, 187, 197-198
- Synthroid (levothyroxine), 165, 166
- Systemic lupus erythematosus
 - syndrome resembling. *See* Lupus-like syndrome
- Tablet(s)
 - biopharmaceutic characteristics of, 65, 65-67
 - buccal
 - disintegration test for, 73
 - coated. *See also* Enteric-coated tablet(s)
 - biopharmaceutic characteristics of, 67-68
 - disintegration test for, 72-73
 - compaction of micronized particles in, 52
 - disintegration test for, 72
 - film-coated, 67
 - methods of production of, 65
 - press-coated, 67-68
 - sublingual
 - disintegration test for, 73
 - sugar-coated, 67
- Tamoxifen
 - rectal administration of, 115
 - bioavailability after, 171

- Tamoxifen (*cont'd.*)
 warfarin interaction with, 331
- Temazepam
 pharmacokinetics of
 age and, 248
 gender differences in, 253
- Tenoxicam
 aspirin interaction with, 310
- Terbutaline
 inhalation of, 97
 intestinal metabolism of, 158, 228-229
 prodrug of, 43
- Testosterone
 brain-selective delivery of, 190
- Testosterone cypionate
 intramuscular injection of
 prolonged-release formulation for, 136
- Testosterone enanthate
 intramuscular injection of
 prolonged-release formulation for, 136
- Testosterone propionate
 intramuscular injection of
 prolonged-release formulation for, 136
 topical application of, 110
- Tetracycline(s)
 antacids' interaction with, 306
 bioequivalence problems with, 169
 bismuth subsalicylate interaction with, 307
 calcium complexation with, 33-34, 57
 changes in gut bacteria due to
 bioavailability of other drugs and, 154
 digoxin interaction with, 308
 ferrous sulfate interaction with, 306
 food's effects on absorption of, 33-34, 57
 intramuscular injection of
 complications of, 91
 rectal administration of, 114
- Tetracycline hydrochloride
 bioequivalence problems with, 169
- 3,4,5,6-Tetrahydrouridine (THU)
 enzyme inhibition by, with cytarabine therapy, 217
- Theophylline
 absorption of
 circadian variation in, 129-130
 food and, 308-309
 allopurinol interaction with, 324
 bioequivalence problems with, 169-170
 cimetidine interaction with, 328, 329t
 diltiazem interaction with, 329
 erythromycin interaction with, 330
 excretion of, in milk, 213
 half-life of
 diet's effects on, 336
 in obesity, 240
 hepatic blood flow alterations due to
 drug interactions due to, 332
 individualization and optimization of dosage
 regimen for, 370-371
 pharmacokinetics of
 age and, 242t, 243, 245, 248
 concentration-dependent, 225-226
 in cardiovascular disease, 296
 in cystic fibrosis, 300-301
 in liver disease, 283
 in obesity, 239
 in smokers, 248, 335
 in viral respiratory infections, 298
 influenza vaccine's effects on, 299
 phenytoin interaction with, 319-320
 prolonged-release formulation of, 127-130, 129t, 129, 131
 food's effects on, 135, 135
 propranolol interaction with, 326
 quinolone antibiotic interaction with, 330
 rectal administration of, 114
 bioavailability after, 171
 renal clearance of
 urine flow rate and, 209, 209
 therapeutic concentration range for, 180t
 Therapeutic concentration range, 180, 180t, 346
- Therapeutic drug monitoring, 371-372
 in patients with impaired drug-binding, 293
 in saliva, 354
 indications for, 346
- Therapeutic effectiveness. *See also* Response
 plasma concentration and, 179, 179-180
- Therapeutic index
 defined, 125
 dosing interval and, 125
- Thiamine
 bioavailability of
 dose and, 26-27
- Thiopental
 distribution volume of, in obesity, 238
 duration of effect of
 redistribution and, 192
 pharmacokinetics of, in elderly patients, 250-251
- Thioridazine
 phenytoin interaction with, 326
- Thymine
 intestinal transport of, 26
- Thyroid disease
 pharmacokinetic variability due to, 297-298
- Thyroxine. *See also* Levothyroxine
 cholestyramine adsorption of, 58
- Timolol
 enzyme inhibition by
 drug interactions due to, 326
 pharmacokinetics of
 genetic factors and, 262
 topical application of, to eye
 systemic absorption after, 101
- Tissue binding, 201
 age-related changes in, 248
 disease's effects on, 290
 pharmacokinetic implications of, 292
- Tissue compartment, 14, 15
- Tobramycin
 absorption of, in malabsorptive states, 36
 individualization and optimization of dosage
 regimen for, 351-353
 pharmacokinetics of, in obesity, 238
- Tolbutamide
 bioavailability of
 tablet formulation and, 66, 67
 bioequivalence problems with, 170-171
 chloramphenicol interaction with, 323
 food's effects on absorption of, 34
 pharmacokinetics of
 age and, 242t
 in cholestasis, 286
 in liver disease, 291
 plasma protein binding of
 in liver disease, 289
 saliva/plasma concentration ratio for, 212
 sulfonamide interaction with, 325
 variable effect of, 234
- Tolbutamide sodium
 absorption of, 49
- Tolerance
 acquired, 182

- pharmacodynamic, 182
- pharmacokinetic, 182
- Tolifenamic acid
 - absorption of, during migraine attack, 31
- Total body water
 - estimation of, 194
- Toxicity. *See also* Adverse drug reaction(s)
 - metabolites as source of, 218-220
- Transcortin
 - drug binding by, 196
- Transdermal medication
 - prolonged-release, 139-142
- Trapezoidal rule, 377, 377t, 378
- Trauma
 - plasma α_1 -acid glycoprotein concentrations after, 290, 290
- thermal
 - pharmacokinetic variability due to, 299-300
- Trazodone
 - pharmacokinetics of, in obesity, 239
- Triamcinolone acetonide
 - intramuscular injection of
 - prolonged-release formulation for, 136
 - topical
 - bioequivalence problems with, 172
- Triamcinolone diacetate
 - intramuscular injection of
 - prolonged-release formulation for, 136
- Triamterene
 - food's effects on absorption of, 35
 - hydrochlorothiazide with
 - absorption of, from capsule vs. tablet, 64
 - bioequivalence problems with, 165
 - pharmacokinetics of
 - in elderly patients, 246-247
 - in liver disease, 285
- Triazolam
 - pharmacokinetics of
 - age and, 248
- Triclofos
 - warfarin interaction with, 310
- Tricyclic antidepressant(s). *See also* particular drugs
 - concentration-response relationship for, 182
 - dosing interval for, 13
 - individualization and optimization of dosage,
 - regimens for, 366-370
 - pharmacokinetics of, in elderly patients, 251
 - toxicity of, 368-369
- Trihexyphenidyl
 - levodopa interaction with, 307
- Triiodothyronine
 - intramuscular injection of, 90
- Trimethoprim-sulfamethoxazole (TMP-SMZ)
 - warfarin interaction with, 325
- d-Tubocurarine
 - volume of distribution of, in children, 241
- Tubular reabsorption, 203, 204, 207-209
 - active, 209
 - age-related changes in, 246
 - effects of, on renal clearance, 204-205
 - renal clearance values indicating, 204
 - tubular secretion, 203, 204, 206-207
 - age-related changes in, 245, 246
 - effects of, on renal clearance, 204-205
 - factors affecting, 205
 - renal clearance values indicating, 204
- Ultrafiltration
 - plasma protein binding studies using, 197
- Uracil
 - intestinal transport of, 62
- Uric acid
 - tubular reabsorption of, 209
- Urinary excretion
 - bioavailability estimation from, 9, 147
 - mean residence time determination from, 20
- Urine flow rate
 - calculation of, for crystalluria prevention, 209
 - tubular reabsorption and, 209, 209
- Urine pH
 - diurnal variation in, 208
 - drug-induced modification of
 - interactions due to, 310-311
 - factors affecting, 207
 - tubular reabsorption and, 207-209, 208
- Vaginal administration, 101-102
- Valproate
 - rectal administration of, 116-117
- Valproic acid
 - enzyme inhibition by
 - drug interactions due to, 327, 327t
 - individualization and optimization of dosage
 - regimen for, 358-359
 - interactions of, with other anticonvulsants, 310, 318, 321, 327, 327t
 - pharmacokinetics of
 - in elderly patient, 247-248
 - in pregnancy, 255
 - plasma protein binding of
 - in liver disease, 290
 - in renal disease, 289, 289
 - teratogenic effects of, 219-220
 - enzyme inhibition and, 327
- Vancomycin
 - dosage regimen for
 - adjustment of, in renal disease, 277
 - individualization and optimization of, 353
 - pharmacokinetics of
 - after burn injury, 299-300
 - in obesity, 238-239
- Vasoconstrictor, assay
 - for bioavailability evaluation, for topical
 - glucocorticoids, 171-172
- Vasopressin
 - azopolymer-coated, 71
- Vecuronium
 - pharmacokinetics of, in children, 241
- Verapamil
 - digoxin interaction with, 316, 329
 - enzyme inhibition by
 - drug interactions due to, 329
 - metabolism of
 - stereoselectivity in, 223
 - pharmacokinetics of
 - age and, 250
 - in obesity, 239
 - time-dependent, 228
 - phenobarbital interaction with, 320
- Vinblastine
 - implantable infusion pump for, 138
- Viral illness
 - pharmacokinetic variability due to, 298-299
- Volume of central compartment
 - apparent
 - calculation of, 16
- Ulceration
 - due to drugs lodging in esophagus, 30

Volume of distribution, 194-195

- actual, 194
- apparent, 2, 194-195
 - body weight and, 236
 - calculation of, 16
 - changes in, in disease, 291
 - estimation of, using moment analysis, 19
 - in obesity, 237, 238
 - of metabolites, 220
- half-life and, 19
- in vascular space, 187

Warfarin

- binding of
 - drugs interfering with, 309
 - in renal disease, 288
 - intersubject variability in, 197
- carbamazepine interaction with, 321
- chloral hydrate interaction with, 310
- cholestyramine interaction with, 58, 211
- cimetidine interaction with, 327-328
- clearance of
 - free plasma concentration and, 200, 200
 - concentration-response relationship for, 182
- disulfiram interaction with, 323
- enoxacin interaction with, 330
- free concentration of
 - drug effects and, 199

individualization and optimization of dosage regimen for, 364-365, 365

- metabolism of
 - stereoselectivity in, 222
- metronidazole interaction with, 325
- pharmacokinetics of, in anesthesiology residents, 338
- phenobarbital interaction with, 319, 320
- phenylbutazone interaction with, 324
- propafenone interaction with, 331
- rifampin interaction with, 321, 322
- secobarbital interaction with, 320
- sulfapyrazole interaction with, 324
- tamoxifen interaction with, 331
- triclofos interaction with, 310
- trimethoprim-sulfamethoxazole interaction with, 325
- variable effect of, 234

Weight. See Body weight

Wet granulation

 tablet production by, 65

Wetting agent(s)

- dissolution and, 52, 52t
- in capsule dosage forms, 64

Zero moment of concentration-time curve, 17

Zero-order release, 126

 dosage form for, 132-133, 132-134

Zemepirac

 irreversible binding of, 199

Zoxazolamine

 individual differences in response to, 176-177, 177