

Index

Page numbers in *italics* refer to figures, those in **bold** refer to tables.

- 2C-B **430**, 439, 439
 2C-D **430**, 439, 440
 2C-E **430**, 439, 440
 2C-I **430**, 439, 440
 2C-T-2 **430**, 439, 440, 441
 2C-T-7 **430**, 439, 441
- a**
- abacavir 274, 396
 acetaldehyde 44
 – and alcoholism risk 499, 500
 – metabolism of 510, 511
 – as product of ethanol metabolism 493, 497, 498, 498, 504, 505, 510
 – production by gastric bacteria 503
 – toxicity and carcinogenicity 493, 499–501, 503, 642
 acetaldehyde dehydrogenase (ALDH) 365, 493, 498, 502, **507**, 510, 511
 – polymorphisms 261, 499, 511
 acetaminophen, *see* paracetamol (acetaminophen)
 acetazolamide 188, 344, **345**
 acetone 170, 504, 505, **507**
 acetonitrile 643
 acetylaminofluorene **507**
 2-acetylaminofluorene 643
 N-acetylation 18, 134, 396
 acrolein 643
 acrylamide 613, 614, 643, 644
 acrylonitrile 644, 645
 acyclovir 390
 adefovir 390
 adrenaline 18
 adrenergic receptor agonists 337
 – α_1 -selective adrenergic receptor agonists **337**, 337
 – α_2 -selective adrenergic receptor agonists **338**, 338, 339, 339, 403
 adrenergic receptor antagonists 339, **340**
 – α_1 -selective adrenergic receptor antagonists 339, 340, 341
 – α_2 -selective adrenergic receptor antagonists 340, **341**, 342
 – β -selective adrenergic receptor antagonists 342, **343**, 344
 adverse drug reactions (ADRs) 259
 aflatoxins 8, **507**, 569, 570, 614, 615, 615
 age influence
 – on ADH activity 503
 – on CES2 177
 – on drug metabolism 293
 – on insecticide metabolism 695
 – on MEOS activity 504
 – on nicotine metabolism 478
 – on SULT1A1 134
 – on UGT1A7 93, 94
 agomelatine 306
 AhR/ARNT complex 33
 – possible impact on estrogen receptors 675
 – regulation of CYPs 33, 225, 226, 231–233, 612
 – regulation of *UGT1A* genes 95, 96, 96, 98
 alacepril 332
 alcohol, *see* ethanol
 alcohol dehydrogenase (ADH)
 – ethanol metabolism 295, 493, 495, 497–500, 498
 – – gastric first-pass metabolism (FPM) 502, 503
 – human genes **496**

- inhibition of 502
- retinol metabolism 501, 502, 502
- THC metabolism 433
- aldehyde oxidase (AO) 10, 11
- aldo-keto reductases (AKRs) 14, 372
- alfentanil 293, 417
- alkaloids 532, 533, 535, 536
- allopurinol 12, 370
- alprazolam 310, 592, 593
- amikacin 380, 381
- amiloride 347, 347
- amine oxidases 10, 11
- amino acid conjugation 19, 20
- 4-aminobiphenyl 507, 644
- 2-aminofluorene 507
- aminoglycosides 380, 381
- amisulpride 309
- amitriptyline 266, 302, 405, 410, 411, 507, 593
- amlodipine 349, 350
- ammonia 641, 644
- amoxicilline 387
- amphetamine 11, 311, 429, 430, 432, 434
 - derivatives 435–439, 436
- amphotericin B 386, 388
- anastrozole 373
- androstosterone 126, 131
- angiotensin-converting enzyme (ACE) 332
 - ACE inhibitors 332–334, 333, 334
- angiotensin II receptor type 1 blockers (ARBs) 334–337, 335, 336
- anidulafungin 386, 388
- aniline 446, 507
- o*-anisidine 644
- anthocyanins 544–546, 551
- anthracyclines 9, 214, 372
- anthraquinones 88
- anti-HIV agents 391–393
- anti-inflammatory agents 17, 266, 408–410, 535, 564, 565, 621
- anti-pain drugs, *see* painkillers
- antiarrhythmics 349–351, 350, 351
- antibacterial agents 266, 295, 379, 572, 573
 - aminoglycosides 380, 381
 - β -lactams 383–386
 - flavonoids 564
 - vancomycin 382, 383
 - *see also* antimicrobial agents
- antibiotics 387
 - antibacterial agents, *see* antibacterial agents
 - as anticancer drugs 371, 372
 - antifungal agents 386, 388, 389, 564, 619
- anticancer drugs 13, 365
 - alkylating drugs
 - busulfan 366, 367
 - ethyleneimines 366
 - melphalan 366
 - methylhydrazines 367
 - oxazaphosphorine 365, 366
 - platinum-containing agents 367
 - antimetabolites
 - cytidine analogs 368, 369
 - folic acid antagonist 367, 368
 - purine analogs 369, 370
 - pyrimidine analogs 368
 - chemotherapy resistance, overcoming 214, 215
 - endocrine therapy
 - aromatase inhibitors 373
 - histone deacetylase inhibitor 373
 - proteasome inhibitor 375
 - selective estrogen receptor modulator 372, 373
 - tyrosine kinase inhibitors 373, 374
 - natural products
 - camptothecin analogs 371, 372
 - taxanes 370, 371
 - vinca alkaloids 370
 - St John’s Wort 587
- anticoagulants 293, 331, 351, 354, 620
- antiplatelet drugs 352, 353, 353
 - heparin 352
 - vitamin K antagonists 352
- anticonvulsants 266, 311–313, 366, 367, 592
- antidepressants 4, 230, 266, 301, 302, 507
 - agomelatine 306
 - bupropion 267, 305
 - duloxetine 305
 - MAO inhibitors 306
 - milnacipran 305
 - minaprine 305
 - nefazodone 305
 - as painkillers 410–412
 - reboxetine 305
 - SSRIs 303–305, 304
 - St John’s Wort 306, 587
 - tricyclic 302, 303
 - venlafaxine 305
- antiepileptics 179, 266, 388, 405, 406, 415
- antifungal agents 386, 388, 389, 564, 619
- antimetabolites 367–370
- antimicrobial agents 379, 397, 398
 - aminoglycosides 380, 381
 - anti-HIV agents 391, 392
 - antibacterial agents, *see* antibacterial agents

- as anticancer drugs 371, 372
 - antifungal agents 386, 388, 389, 564, 619
 - antiviral agents 14, 190, 389–393, 563, 564, 587
 - β -lactams 383–386, 387
 - flavonoids 564
 - key issues 397
 - pharmacogenetics 393, 394, 394, 395, 396, 397
 - vancomycin 382, 383
 - antimigraine drugs 313
 - antimony compounds 646
 - antiplatelet agents 173, 174, 352, 353, 565
 - antipsychotics 263, 306
 - atypical antipsychotics 307, 308, 308
 - butyrophenones and related compounds 307
 - phenothiazines and thioxanthenes 306, 307
 - antiviral agents 14, 190, 389–393, 563, 564, 587
 - *see also* antimicrobial agents
 - apigenin 550, 557–559, 562, 564, 565
 - CYP interaction 560, 568, 569, 624
 - cytoprotection 567
 - cytotoxicity 563, 567
 - aripiprazole 309
 - armamentarium 384, 389
 - aromatase inhibitors 373, 568, 619
 - arrhythmias 169, 331, 342, 349
 - arsenic and arsenic compounds 645
 - artemisinin 267, 527, 528
 - aryl hydrocarbon receptor (AhR) 229, 271, 656
 - AhR/ARNT complex, *see* AhR/ARNT complex
 - binding with flavonoids 558, 559
 - crosstalk with Nrf2 98
 - crosstalk with RAR 232
 - crosstalk with TR 232
 - impact on estrogen receptors 675–677
 - induction of UGT enzymes 16
 - interactions with flavonoids 558–560
 - interactions with PCBs 658, 677, 678
 - regulation of CYPs 225–227, 229, 231–233, 612
 - aryl hydrocarbon receptor nuclear translocator (ARNT) 33, 232, 675
 - AhR/ARNT complex, *see* AhR/ARNT complex
 - arylhydroxamic acids 134
 - asbestos 645, 646
 - asenapine 309
 - aspirin 176, 408, 502, 503, 507
 - atazanavir 83, 84, 86, 88, 392, 393
 - atherosclerosis 82, 331, 353, 561, 627, 628
 - atomoxetine 311
 - atorvastatin 88, 234, 355, 356, 357, 357, 593
 - and Gilbert–Meulengracht syndrome 83, 84
 - atrazine 676, 677
 - atrial natriuretic peptides (ANPs) 347
 - azacitidine 369
 - azathioprine 12, 12, 19, 268
 - azoles 386, 388
- b**
- β -blockers 293, 342, 343, 344
 - β -lactams 380, 381, 383–386, 387
 - barbiturates 51, 267, 310, 507
 - benazepril 332
 - benzene 507, 646, 647
 - benzidine 69, 647
 - benzil derivatives 171, 172, 172
 - benzo[a] pyrenes
 - toxicity and carcinogenicity 507, 612, 613, 657
 - and *UGT1A1* gene 79, 86
 - and *UGT1A3* gene 87
 - and *UGT1A7* gene 88
 - benzodiazepines 226, 237, 293, 309, 310
 - benzodioxolylbutanamine (BDB) 430, 436, 436–438
 - benzothiazepines 349
 - benzylpiperazines (BZP) 431, 444, 445, 445
 - bergamottin 295, 532, 534, 534, 571, 623
 - I3,II8-biapigenin 571, 591, 591
 - bile acid sequestrants 354
 - bile acids 87, 97, 98, 126, 226, 237, 238, 530, 629
 - biosynthesis of 522, 524, 530
 - bilirubin 82, 83, 99, 100, 225
 - glucuronidation of 69, 78, 79, 269
 - hyperbilirubinemia, *see* hyperbilirubinemia
 - bilirubin transferase 68, 82
 - biological availability of drugs 3, 4
 - biotoxification 287, 290, 509, 694
 - blood pressure 331, 332, 332
 - hypertension 13, 31, 82, 331, 338, 342
 - boceprevir 390
 - bortezomib 366, 374
 - brain
 - drug transport into 211, 214
 - *SULT4A1* expression 127
 - breast cancer 558, 567, 571, 674, 677
 - and *SULT1A1**2 gene 132
 - treatment 372, 373

- and *UGT1A1* gene 87
 - 4-bromo-2,5-dimethoxy-methamphetamine (MDOB) 430, 438, 439
 - 4-bromo-2,5-dimethoxyamphetamine (DOB) 430, 438, 439
 - bromobenzene 507
 - bromophenyl-dione 172
 - bufuralol 591
 - buprenorphine 79, 83, 84, 406, 416
 - bupropion 267, 305, 482
 - buspiron 310, 311
 - busulfan 366, 367
 - 1,3-butadiene (vinyl ethylene) 155, 647
 - butanol 504, 507
 - butorphanol 416
 - butylone 431, 442, 442
 - butyrophenones 306, 307
- c**
- cadmium compounds 647, 648
 - caffeine 507, 507, 533, 535, 592, 593, 594, 626
 - calcium carbimide 507
 - calcium channel blockers 331, 349–351, 350, 351
 - camptothecin analogs 371
 - cancer
 - anticancer drugs, *see* anticancer drugs
 - breast cancer, *see* breast cancer
 - carcinogens, *see* carcinogens
 - colorectal cancer (CRC), *see* colorectal cancer (CRC)
 - drug transporters and chemotherapy resistance 214, 215
 - environmental pollutant-associated, *see* carcinogens
 - ethanol-associated 493, 500, 501, 503, 506, 511
 - and fatty acids 621, 622
 - flavonoid impact on 568–570
 - food-associated 613, 614, 626
 - pancreatic cancer 94, 95
 - photodynamic therapy 587
 - and *UGT1A1* gene 82, 83, 86, 87, 89–92
 - and *UGT1A7* gene 93–95
 - candesartan 335, 335
 - cannabinoids 528
 - canrenone 348
 - capecitabine 368
 - captopril 332, 333
 - carbamate insecticides 685, 686, 687
 - interaction with xenobiotics 695
 - interactions with drugs 175
 - metabolism of 688–692, 689, 691, 693
 - carbamazepine 226, 234, 274, 312, 405, 415, 593, 618
 - carbapenems 383–386
 - carbaryl 686, 688, 689, 691, 695
 - carbenium 7, 17, 643, 644
 - carbofuran 686, 687, 688
 - carbohydrates 622
 - carbon dioxide 547, 550, 641, 644, 651
 - carbon monoxide 480, 641, 644, 648, 649, 651
 - carbon tetrachloride 507, 648
 - carbonic anhydrase inhibitors 344, 345
 - carbonic anhydrases 188
 - carbonyl reductases 14, 15
 - carboplatin 367
 - carbosulfan 686, 688, 689, 691
 - carboxyesterases 3, 371
 - carboxylesterases 165
 - activators 170
 - catalytic mechanism 168, 169
 - classification and structure 166
 - – human carboxylesterases 166, 167, 167
 - – salient features 167
 - – secondary and crystal structure 167, 168
 - drug-insecticide interactions 175
 - human-animal comparisons 175, 176
 - – ontogenic expression 177
 - – regulated expression 177
 - – species-specific hydrolysis 176, 177
 - – tissue distribution 176
 - inhibitors 171, 172
 - interaction with CYPs 173, 174
 - interaction with UGTs 174, 175
 - interactions with drug transporters 175
 - pharmacogenetics 172, 173
 - polymorphisms 173
 - structures of some drugs metabolized by 166
 - substrate specificity 169, 170, 170
 - substrates metabolized 165
 - – heroin 418
 - – insecticides 175, 692, 693
 - – irinotecan 289
 - – ramipril 334
 - carcinogens 154, 507
 - acetaldehyde 493, 499, 503, 511, 642
 - acetylaminofluorene 507, 643
 - acrolein 643
 - acrylamide 613, 614, 643, 644
 - acrylonitrile 644, 645
 - activation by flavonoids 568–570
 - aflatoxins 8, 507, 569, 570, 614, 615, 615
 - 4-aminobiphenyl 507, 644

- 2-aminofluorene 507
- o-anisidine 644
- antimony compounds 646
- arsenic and arsenic compounds 645
- asbestos 645, 646
- benzene 646, 647
- benzidine 647
- benzo[a] pyrenes 507, 612, 613, 657
- 1,3-butadiene 155, 647
- cadmium compounds 647, 648
- carbon tetrachloride 648
- chloroform 649
- chloroprene 649, 650
- chromium (VI) compounds 650
- cobalt and cobalt compounds 650, 651
- 1,4-dichlorobenzene 651
- dichloromethane 651, 652
- 1,3-dichloropropene 651
- dimethylhydrazine 503, 507, 652
- 1,1-dimethylhydrazine 652
- ethylene oxide 155, 652
- formaldehyde 652, 653
- fungal toxins 614, 615, 615
- heptachlor 653
- hexachlorobenzene 653, 654
- hydrazine 654
- lindane 655
- methyl bromide 155
- nitrobenzaldehyde 653
- nitrosamines 7, 470, 481, 483, 507, 509, 614, 656
- polychlorinated biphenyls 658
- polychlorinated dioxins and furans 658, 659
- polycyclic aromatic amines 611–613, 626
- polycyclic aromatic hydrocarbons 88, 612, 613, 657, 658
- pyrrolisates 507, 570
- styrene and styrene oxide 659
- tetrachloroethylene 660
- vinyl chloride 660
- cardiovascular disease 180, 182
 - and cholesterol 626, 627, 628
 - and fatty acids 621, 622
 - and flavonoids 565, 624
 - and isothiocyanates 625, 626
 - and *UGT1A1* gene 82
- cardiovascular drugs 331
 - adrenergic receptor agonists 337
 - α_1 -selective adrenergic receptor agonists 337, 337
 - α_2 -selective adrenergic receptor agonists 338, 338, 339, 339
 - adrenergic receptor antagonists 339, 340
 - α_1 -selective adrenergic receptor antagonists 339, 340, 341
 - α_2 -selective adrenergic receptor antagonists 340, 341, 342
 - β -selective adrenergic receptor antagonists 342, 343, 344
 - antiarrhythmics 349–351, 350, 351
 - anticoagulants 351, 354
 - antiplatelet drugs 352, 353, 353
 - heparin 352
 - vitamin K antagonists 352
 - cholesterol-lowering drugs 353
 - bile acid sequestrants 354
 - cholesterol uptake inhibitors 354
 - fibrates 354, 355
 - statins 355, 356, 357, 357
 - diuretics 342, 344
 - carbonic anhydrase inhibitors 344, 345
 - inhibitors of renal epithelial Na⁺ channels 347, 347, 348, 348
 - mineralcorticoid receptor antagonists 348, 349
 - Na⁺–K⁺–2Cl⁻ symport inhibitors 345, 346
 - nonspecific cation channel inhibitors 347
 - osmotic diuretics 344, 345
 - thiazide or thiazide-like diuretics 345, 346
 - RAAS, control of
 - ACE inhibitors 332–334, 333, 334
 - ARBs 334–337, 335, 336
- β -carotene 522, 525, 530, 618
- carotenoids 522, 616–618
- carvedilol 343
- caspofungin 386, 388
- catalase 493, 498, 510, 642
- catechol-O-methyltransferase (COMT) 18, 19, 314, 436, 437, 548, 549, 552
- catecholamines 121, 124, 125, 130, 339, 342
- cathinones 431, 441, 442, 442
- cation channel inhibitors 347
- cefazolin 187, 188
- cefazoline 387
- cefepime 384, 385, 387
- ceftazidime 387
- ceftriaxone 384, 387
- celecoxib 404, 410
- central nervous system drugs 301, 314, 315
 - agents for dementia and cognitive enhancers 313
 - anticonvulsants and mood stabilizers 311–313

- antidepressants 301, 302
- – MAO inhibitors 306
- – other recent antidepressants 305, 306
- – SSRIs 303–305, 304
- – tricyclic antidepressants and structurally related compounds 302, 303
- antimigraine drugs 313
- antipsychotics 306
- – atypical antipsychotics 307–309, 308
- – butyrophenones and related compounds 307
- – phenothiazines and thioxanthenes 306, 307
- other drugs 314
- psychostimulants 311
- tranquilizers and hypnotic agents 309–311
- cephalosporins 383–386, 507
- cerivastatin 83, 84, 356
- chenodeoxycholic acid (CDCA) 97, 98
- chlomethiazole 507
- chloral hydrate 507
- chloramphenicol 99, 507
- chlordane 676
- chlormethiazol 509
- 4-chloro-2,5-dimethoxyamphetamine (DOC) 430, 438, 439
- chloroform 648, 649
- 1-(3-chlorophenyl)piperazine (mCPP) 431, 444, 445, 445, 446
- chloroprene 649, 650
- chlorothiazide 345, 346
- chlorpromazine 306, 502, 507
- chlorpyrifos 184, 685, 686, 695–697
- metabolism of 688, 689, 689, 690, 690, 691, 692
- cholesterol 226, 524, 529, 530, 626–628, 627
- as *SULT* substrate 126
- cholesterol-lowering drugs 353
- bile acid sequestrants 354
- cholesterol uptake inhibitors 354
- fibrates 354–355
- statins 355, 356, 357, 357
- cholesterol uptake inhibitors 354
- cholinesterases 171, 188, 189, 189
- chromium (VI) compounds 650
- chrysin 546, 547, 550, 558–561, 568, 624
- cilastatin 387
- cilazapril 332
- cimetidine 502, 503, 507, 572
- 1,4-cineole 527
- 1,8-cineole (eucalyptol) 522, 526, 526, 527
- ciprofloxacin 507
- cisplatin 367
- citalopram 266, 303, 304, 405, 413
- citral 524, 525
- clarithromycin 266, 295
- Clark theory 229, 230
- clavulanic acid 384
- clobazam 310
- clomipramine 302
- clonidine 338, 338, 339
- clopidogrel 166, 171, 174, 176, 290, 352, 353, 353, 354
- and CYPs 173, 266, 274, 444
- clozapine 9, 11, 230, 307, 308, 308, 507
- coactivator proteins 33, 231
- cobalt and cobalt compounds 650, 651
- cobicistat 392
- cocaine 169, 170, 430, 432, 432, 433, 509
- codeine 266, 290, 406, 416, 417, 533, 535
- cognitive enhancers 313
- colchicine 533, 535
- colorectal cancer (CRC) 83, 269, 644
- and *UGT1A* genes 80, 85, 87, 93
- COMT inhibitors 314
- congestive heart failure (CHF) 331, 342
- conjugating enzymes 15–20
- conjugation reactions 4
- constitutive androstane receptor (CAR) 97, 528, 616, 672
- and PXR 228
- regulation of CYPs 33, 226, 227
- – CYP1As 231
- – CYP2A6 234
- – CYP2B6 234, 235, 235
- – CYP2C subfamily 236
- – CYP3A subfamily 237, 238
- and RXR- α 226
- coumarin 88, 478–480, 532, 532, 534, 623, 624
- Crigler–Najjar syndrome 68, 72, 73, 77, 78, 79, 99, 100, 269
- cyclooxygenase-2 selective inhibitors 404, 405, 410
- cyclooxygenases (COXs) 6, 8, 8, 9, 18, 559–562, 621
- cyclophosphamide 9, 267, 365, 366, 507, 643
- cyclosporin A 269
- cyclosporine 388, 532, 532, 594, 619, 622, 625
- cypermethrin 686, 687, 694
- cystic fibrosis 208, 380
- cytarabine 368, 369
- cytidine analogs 368, 369
- cytochromes P450 (CYPs) 6–8
- carboxylesterases, interaction with 173, 174

- catalytic mechanisms
 - alternative mechanisms proposed 42, 43, 44
 - general mechanism 40–42, 41
 - kinetic deuterium isotope effects 44–46
 - catalytic selectivity 45–47
 - clinical issues 48, 50, 51
 - drug metabolism 48, 49, 50, 51
 - P450s deficiencies 50
 - CYP2A6 activity and nicotine metabolism 481, 482
 - difference spectrum 28
 - drug-drug interaction 48, 51, 224, 226, 237, 263, 355, 374
 - ethanol metabolism 503, 504–506, 505
 - factors affecting 292–296
 - functions 30, 30, 31
 - gene organization 30, 30–32
 - genetical genomics 276
 - inhibitors of human P450 enzymes 49
 - knowledge about, use of 52
 - NADPH-P450 reductase interaction 37, 38
 - nomenclature 29, 29, 30, 275
 - oxidative stress 47, 48
 - polygenic inheritance 270, 271
 - polymorphisms 35–37, 51, 263, 266–270, 696, 697
 - and nicotine metabolism 471, 472–475, 476
 - websites 36, 471
 - protein structures 37–40, 38, 38, 39
 - and reactive oxygen species (ROS) 48, 232
 - regulation of 32
 - by AhR 225–227, 229, 231–233, 612
 - by AhR/ARNT complex 33, 225, 226, 231–233, 612
 - by CAR 33, 226, 227, 231, 234–238
 - epigenetic 34
 - by ER 227, 231–233, 235
 - by GR 227, 232, 234–236, 238
 - by HNFs 33, 34, 234–238, 271
 - by kaempferol 569, 624
 - by ligands 229, 230
 - by LXR 235, 238, 530
 - by nuclear receptors 97, 227–229, 235
 - post-translational 34, 35
 - by PPAR- α system 33, 227, 232, 271
 - by PR 231
 - by prostaglandin 231
 - by PXR 33, 226, 234–238, 292, 620
 - by quercetin 624
 - by RAR 227, 232
 - by steroid receptors 227
 - by TR 227, 232
 - transcriptional 32, 32–34
 - see also* transcriptional regulation of human CYPs
 - by VDR 227, 235, 236, 237
 - by XREs 225, 231–233, 235, 236
 - research history 27–29
 - role in metabolism of specific drugs/substances, *see specific drugs/substances*
 - toxic species from biotransformation 7, 8
 - transcriptional regulation 32, 32–34
 - in humans, *see* transcriptional regulation of human CYPs
 - *in vitro* marker activities for some human P450s 50
 - websites 29, 36, 471, 476
- d**
- dactinomycin 371
 - dapsone 9, 18, 396
 - daptomycin 383, 387
 - dasatinib 373, 374
 - daunorubicin 9, 14, 15, 372, 555
 - debrisoquine 36, 50, 51, 263, 336, 595
 - decitabine 369
 - dehydroepiandrosterone (DHEA) 17, 126, 131, 234
 - dehydroepiandrosterone sulfate (DHEAS) 126
 - deltamethrin 176, 686, 687, 688
 - dementia, agents for 313
 - deprenyl 306
 - designer drugs
 - amphetamine derivatives 430, 435–439
 - cathinones 431, 441, 442
 - phencyclidine derivatives 431, 443, 444
 - phenethylamines (2Cs) 430, 439–441
 - piperazines 431, 444–446
 - pyrrolidinophenones 431, 446–450
 - tryptamines 431, 450
 - desipramine 302, 405, 412
 - desmethylclomipramine 302
 - dexamethasone 151, 176, 177, 232, 234, 236, 238
 - dexfenfluramine 311
 - dexmedetomidine 403, 404
 - dextromethorphan 438, 592, 595
 - dextromoramide 417
 - dextropropoxyphene 406, 417
 - diacetylmorphine (heroin) 169, 170, 406, 417, 418, 430, 432, 432
 - diamine oxidase (DAO) 11
 - diamorphine (heroin) 406, 417, 418

- diazepam 267, 310, 507
 diazinon 685, 688, 689, 692
 diazoxon 696, 697
 1,4-dichlorobenzene 651
 dichlorodiphenyltrichloroethane (DDT)
 674, 677, 688
 dichloromethane 155, 156, 651, 652
 1,3-dichloropropene 651
 diclofenac 404, 408, 591
 dieldrin 674
 diethylstilbestrol (DES) 673
 digoxin 188, 213, 519, 572, 592, 595, 596
 dihydralazine 295
 dihydrocodeine 406, 416, 417
 dihydropyridine dehydrogenase (DPD) 13,
 14
 dihydropyrimidine dehydrogenase (DPD)
 268, 269, 368
 6',7'-dihydroxybergamottin 623, 623, 624
 diltiazem 349, 350
 dimethoate 688, 689
 2,5-dimethoxy-4-methyl-amphetamine
 (DOM) 430, 438, 439
 2,5-dimethoxyamphetamines 430, 436, 438,
 439, 441
 dimethylhydrazine 503, 507, 652
 dioxin-responsive elements (DREs) 225,
 612, 675
 disease influence on drug metabolism 294
 disulfiram 155, 314, 499, 507, 511
 disulfoton 686, 691, 692
 dithienyl ethane-dione 172, 172
 diuretics 342, 344
 – carbonic anhydrase inhibitors 344, 345
 – inhibitors of renal epithelial Na⁺ channels
 347, 347, 348, 348
 – mineralcorticoid receptor antagonists
 348, 349
 – Na⁺–K⁺–2Cl⁻ symport inhibitors 345,
 346
 – nonspecific cation channel inhibitors 347
 – osmotic diuretics 344, 345
 – thiazide or thiazide-like diuretics 345,
 346
 dobutamine 19
 docetaxel 370, 371
 dofcythiotrifluoropropane 172, 172, 173
 donepezil 313
 dopamine 17, 18, 124, 125, 129, 130, 314
 – designer drug effects on 437, 443, 445,
 447
 dothiepin 302, 303
 doxazosin 340
 doxepin 302, 303
 doxorubicin 9, 14, 372, 555
 drug interactions
 – drug-drug 4, 270, 291, 295
 – anti-HIV agents 392
 – and β-lactams 385
 – and CYPs 48, 51, 224, 226, 237, 263,
 355, 374
 – designer drugs 441
 – and DPD 14
 – methods of studying 16
 – and natural product chemicals 520, 521
 – and statins 357
 – and UGTs 16
 – drug-environmental pollutant
 – acetaldehyde 642
 – acetonitrile 643
 – 2-acetylaminofluorene 643
 – acrolein 643
 – acrylamide 643, 644
 – acrylonitrile 644, 645
 – 4-aminobiphenyl 644
 – o-anisidine 644
 – antimony compounds 646
 – arsenic and arsenic compounds 645
 – asbestos 645, 646
 – benzene 646, 647
 – benzidine 647
 – 1,3-butadiene (vinyl ethylene) 647
 – cadmium compounds 647, 648
 – carbon monoxide 648, 649
 – carbon tetrachloride 648
 – chloroform 649
 – chloroprene 649, 650
 – chromium (VI) compounds 650
 – cobalt and cobalt compounds 650, 651
 – 1,4-dichlorobenzene 651
 – dichloromethane 651, 652
 – 1,3-dichloropropene 651
 – 1,1-dimethylhydrazine 652
 – ethylene oxide 652
 – formaldehyde 652, 653
 – heptachlor 653
 – hexachlorobenzene 653, 654
 – hydrazine 654
 – lead and lead compounds 654, 655
 – lindane 655
 – mercury compounds 655, 656
 – mono-nitrogen oxides (NO_x) 656
 – ozone 656
 – parathion 656, 657
 – phthalates 657
 – polychlorinated biphenyls 658
 – polychlorinated dioxins and furans 658,
 659

- polycyclic aromatic hydrocarbons 657, 658
- styrene and styrene oxide 659
- sulfur dioxide 659
- tetrachloroethylene 660
- vinyl chloride 660
- drug-food 295, 611
- carotenoids 617, 618
- flavonoids 570–573, 591, 624, 625
- grapefruit 622–624
- probiotics and prebiotics 628, 629
- protein 620, 621
- riboflavin 620
- thiamine 620
- vitamin D 618, 619
- vitamin E 619
- drug-insecticide 175
- drug-St John's Wort 591, 591, 592, 593–602
- drug metabolism 287, 296
 - ADME processes 288
 - biotransformation 290
 - extrahepatic 290, 291
 - factors affecting 291–296
 - influence on pharmacological activity 289, 290
 - pathways 288, 289
 - research history 287, 288
- drug transporters
 - ABC transporters 200, 208, 209
 - carboxylesterases, interaction with 175
 - and chemotherapy resistance 214, 215
 - and disease 208, 210, 210, 212
 - membrane transport proteins 199, 200
 - pharmacogenomics 215, 269, 270
 - pharmacokinetics 211, 212
 - hepatic transporters 213
 - intestinal transporters 212, 213
 - polymorphisms 269, 270
 - SLC superfamily 200, 201–207
- drugs of abuse 430, 431
 - classic drugs 432–435
 - designer drugs 435
 - amphetamine derivatives 435–439
 - cathinones 441, 442
 - phencyclidine derivatives 443, 444
 - phenethylamines (2Cs) 439–441
 - piperazines 444–446
 - pyrrolidinophenones 446–450
 - tryptamines 450
 - metabolism, importance of understanding 429
- DT-diaphorase 13, 14
- duloxetine 305, 405, 412

e

- echinocandins 386, 388
- efavirenz 234, 267, 268, 393, 394
- eicosanoids 30, 31, 121, 125, 230
- eletriptan 313
- emetine 533, 535
- emtricitabine 390
- enalapril 332
- endocrine disrupting chemicals (EDCs) 671, 673, 678, 679
 - effects on estrogen biosynthesis/ metabolism 676–678
 - effects on estrogen receptors 673–676
- PCBs 677, 678
- endocrine therapy 372–374
- endosulfan 235, 674
- entacapone 314
- entecavir 390
- environmental estrogens, *see* estrogens, environmental
- environmental factors of drug metabolism 294, 295
- environmental pollutants 639, 640, 660, 661
 - air pollutants 641
 - drug-environmental pollutant interactions, *see* drug interactions: drug-environmental pollutant
 - soil pollutants 642
 - types 640, 641
 - water pollutants 642
- enzymes, biotransformation 3, 4
 - classification systems 4–6, 5
 - conjugating enzymes 15–20
 - *see also specific enzymes*
- eosinophil peroxidase 9
- epigenetic regulation 34, 232, 270, 272, 273
- epipodophyllotoxins 372
- eplerenone 348, 349
- epoxide hydrolases (EH) 178, 179
 - catalytic mechanisms 180, 181, 181
 - classification and structure 179, 180
 - comparison of various EHs 181, 182, 182
 - substrates 178
- epoxides 178, 178, 179, 612, 615, 649
- ertapenem 384, 387
- erythromycin 293, 295, 310, 521, 532, 532, 534
 - CYP inhibition 51, 295, 336
- escitalopram 303, 413
- esfenvalerate 176, 177, 686, 688
- esmolol 166, 169
- estazolam 310

- esterases 183, 334, 417, 418, 690, 693
 estradiol 79, 127, 130, 233, 507, 568, 622
 β -estradiol 118, 125, 126
 17 β -estradiol 121, 129, 135, 557, 672, 676, 677
 – and environmental estrogens 674, 677, 678
 estragole 133, 533, 534
 estrogen receptor (ER) 33, 118, 125
 – binding with flavonoids 557, 558
 – EDCs effects on 673–676
 – regulation of CYPs 227, 231–233, 235
 – signalling pathways 672, 673, 673
 estrogens 17, 50, 86, 87, 121, 125, 126, 524, 529
 estrogens, environmental 671, 678, 679
 – effects on estrogen biosynthesis/ metabolism 676, 677
 – effects on estrogen receptors 673–676
 – estrogen receptor signalling pathways 672, 673, 673
 – polychlorinated biphenyls 677, 678
 ezopiclone 310
 ethacrynic acid 155, 345
 ethanol 295, 296, 493, 494
 – absorption 495, 496
 – acetaldehyde metabolism via ALDH 510, 511
 – alcohol-drug interactions 506–510, 507
 – blood alcohol levels 495, 496
 – carcinogenic effects 508, 509, 652
 – content in various alcoholic beverages 494
 – elimination 496, 497
 – gastric first-pass metabolism (FPM) 495, 502, 502, 503
 – human ADHs 496
 – inhibition of retinol metabolism 502
 – metabolic consequences
 – – metabolism via ADH 500, 501, 502
 – – metabolism via MEOS 506, 507
 – metabolism of 44, 47, 295, 296, 497, 498
 – – nonoxidative 510
 – – via ADH 497–502
 – – via catalase 510
 – – via the MEOS 503, 504–510, 505
 – properties and sources 494, 494, 495
 ethinylestradiol 79, 83, 84, 125, 572
 ethylene oxide 155, 652
 ethyleneimines 366
 ethylone 431, 442, 442
 etoposide 372
 etoricoxib 405, 410
 etravirine 393
 eugenol 533, 534
 exemestane 373
 expression quantitative trait loci (eQTL) approach 275, 276
 ezetimibe 83, 84, 87, 354
- f**
- farnesoid X receptor (FXR) 70, 96, 97, 98, 237, 238, 530, 616
 fatty acid ethyl ester synthesis 166
 fatty acids 30, 31, 40, 150, 179, 500, 505, 621, 622
 febuxostat 12
 felbamate 312
 felodipine 571, 622
 fenoterol 9, 339
 fentanyl 417
 fenthion 688, 689, 691, 692
 fentiapril 332
 fexofenadine 269, 507, 596
 fibrates 33, 354, 355, 628
 fisetin 555, 561, 562
 FK3453 12
 flavin monooxygenases (FMOs) 10, 10, 11, 49
 – and anticancer drugs 374
 – and central nervous system drugs 306, 308
 – and cocaine 433
 – and insecticides 691–695
 – and nicotine 468, 469, 477
 flavones 88, 543, 545, 546, 563, 565, 568, 569
 flavonoids 19, 87, 532, 543, 573, 574
 – absorption and metabolism 545
 – – bioavailability 545–547
 – – excretion 550, 551
 – – metabolism 547–550
 – – overall fate in organisms 551–553, 552
 – – pharmacokinetic analyses 553
 – biosynthesis and function in plants 545
 – classification and physicochemical properties 543, 544, 544
 – CYP inducers 237
 – dietary flavonoids health issues 562
 – – antimicrobial agents 563, 564
 – – antioxidant and pro-oxidant properties 562, 563
 – – carcinogen activation 568–570
 – – cytotoxic and cytoprotective effects 566, 567
 – – drug-flavonoid interactions 624, 625
 – – metabolism of endo- and xenobiotics 567, 568
 – – metabolism of endogenous compounds 568

- nutraceutical properties 565, 566
 - other biological activities 564, 565
 - flavonoid-drug interactions 570–573
 - interactions with mammalian proteins 554
 - ATP-binding proteins 555
 - flavonoid-binding receptors 557–559
 - kinases 556, 557
 - molybdoenzymes 12
 - MRPs 555, 556
 - plasma proteins 554, 555
 - redox enzyme activity modulation 559, 660
 - xenobiotic-metabolizing enzymes 560–562
 - in St John's Wort 589, 590
 - SULT inhibitors 17
 - SULT interactions 548, 561, 569, 572
 - flavonols 545, 546, 555, 562
 - flucloxacillin 274, 396
 - flucloxacilline 387
 - fluconazole 16, 386, 388, 389, 564
 - fludarabine phosphate 370
 - flunitrazepam 310
 - 5-fluorouracil 13, 14, 268, 269, 368
 - fluoxetine 303, 304, 405, 413
 - flurbiprofen 87, 404, 408
 - fluvastatin 185, 234, 336, 356, 508
 - flvoxamine 304, 310
 - folic acid antagonist 367, 368
 - food components/supplements 611, 612
 - flavonoids, *see* flavonoids
 - food contaminants
 - acrylamide 613, 614
 - fungal toxins 614, 615, 615
 - nitrosamines 614
 - polycyclic aromatic hydrocarbons and polycyclic aromatic amines 612, 613
 - macronutrients 620
 - carbohydrates 622
 - fatty acids 621, 622
 - protein 620, 621
 - probiotics and prebiotics 628, 629
 - secondary plant metabolites 623, 624
 - caffeine 626
 - cholesterol 626–628, 627
 - from dietary supplements 624, 625
 - glucosinolates and allylsulfides 625, 626
 - from grapefruit juice 622–624, 623
 - vitamins
 - vitamin A, retinoic acid, carotenoids 616–618, 617
 - vitamin D 618, 619
 - vitamin E 619
 - water-soluble vitamins 620
 - formaldehyde 652, 653
 - fosinopril 332, 333
 - fulvestrant 84
 - fungal toxins 614, 615, 615
 - furazolidone 507
 - furosemide 345, 346
- g**
- γ -aminobutyric acid (GABA) receptor 558, 587, 655
 - gabapentin 312, 415
 - galangin 555, 559–561, 624
 - galantamine 313
 - gancyclovir 390
 - gemcitabine 190, 215, 368, 369
 - gemfibrocil 83
 - gemfibrozil 16, 79, 84, 355
 - genetic polymorphisms 260
 - of ADHs 499, 500
 - of ADME genes 261, 262
 - of carboxylesterases 173
 - of CYPs 35–37, 51, 223, 224, 263, 266–268, 270, 271, 471, 472–475, 476
 - of DPD 268, 269
 - and drug metabolism 291, 292
 - and drug toxicity 396
 - of drug transporters 208, 215
 - early examples 260, 263
 - of SULTs 117, 118, 132
 - of TPMT 268
 - of UGTs 71, 269, 477
 - *see also* pharmacogenetics; pharmacogenomics
 - genetical genomics 275, 276
 - genistein 551, 556, 557, 566–568, 619, 675
 - flavonoid-drug interactions 571, 572
 - genome-wide association studies (GWAS) 210, 212, 274, 275, 394, 397
 - gentamicin 380, 381
 - geranial 524, 526
 - geraniol 525
 - gestodene 295
 - Gilbert–Meulengracht syndrome (GMS) 67, 68, 71, 77, 77, 80, 269
 - disposition to drug toxicity 83, 84, 85, 86
 - glabridin 295
 - gliclazide 596
 - glucocorticoid receptor (GR)
 - receptor cross-talk 228, 229
 - regulation of CYPs 232, 234–236, 238

- transcriptional mechanisms 227
 - glucose 6-phosphate dehydrogenase (G6PD) 396
 - glucosinolates 625, 626
 - β -glucuronidase 67, 165, 189, 189, 190
 - glucuronidation 15, 16, 67
 - of bilirubin 68, 69, 78, 79, 269
 - hydrolysis–glucuronidation interaction 174, 175
 - glucuronosyltransferases, *see* UDP-glucuronosyltransferases (UGTs)
 - glutathione S-transferases (GSTs) 18, 147, 148, 520, 692
 - classification and nomenclature 152, 153
 - cystolic GSTs 148–150
 - – GSTA, GSTM, GSTP classes 149
 - – GSTO class 150
 - – GSTS class 149
 - – GSTT class 149
 - – GSTZ class 150
 - induction 151, 155
 - inhibition 155
 - microsomal GSTs 150, 151
 - mitochondrial GSTs 150
 - nomenclature 148, 152, 153
 - polymorphisms 155, 156
 - – GSTA 156
 - – GSTM 156, 156
 - – GSTO 157
 - – GSTP1 157
 - – GSTT 156, 157, 157
 - regulation 151
 - research history 147
 - role in metabolism
 - – of aflatoxin 614, 615
 - – of alkylating drugs 365, 366
 - – of environmental pollutants 644, 646, 652, 654, 660
 - – of insecticides 692
 - – of natural products 520
 - substrates 151, 154
 - glycerin 344, 345
 - glycine conjugation 19, 20
 - glycosidases 189, 546, 548, 551, 553
 - gout 12
 - grapefruit 623
 - CYP interactions 51, 52, 310, 534, 571, 622–624
 - nicotine interactions 480
 - SULT inhibition 17
 - griseofulvin 507
 - guanfacine 338, 338
 - Gunn rats 99
- h**
- haloperidol 14, 307
 - halothane 14, 507, 648
 - harmaline 533
 - harman 533, 535
 - hemes, chemistry of 7
 - hemoxigenase-1 82
 - heparin 352
 - hepatitis, viral 390, 391
 - hepatocellular carcinomas (HCCs) 88, 93, 94
 - hepatocyte nuclear factors (HNFs)
 - miRNA control of 273
 - regulation of CYPs 33, 34, 234–238, 271
 - regulation of *UGT1A* 96, 97
 - heptachlor 653
 - heroin 169, 170, 406, 417, 418, 430, 432, 432
 - herpes virus 14, 390, 587
 - hesperetin 561
 - hexachlorobenzene 653, 654
 - histone deacetylase inhibitor 234, 373
 - HIV 86, 215, 268, 391–393, 563
 - HIV-1 protease inhibitors 213, 268, 269
 - hydralazine 18
 - hydrazine 654
 - hydrocodone 406, 416, 418
 - hydromorphone 406, 418
 - hydropyridines 349
 - 2-hydroxy-estrone 79
 - N*-hydroxy-heterocyclic amines 134
 - hydroxyzine 507
 - hyperbilirubinemia 67, 68, 269, 393
 - animal studies 99–100
 - and cardiovascular disease 82
 - and protease inhibitor therapy 86
 - *UGT1A* gene 71, 77, 78–80
 - hyperforin 235, 521, 588, 588, 591, 591, 592
 - hypericin 587–589, 589, 591, 591
 - hypertension 13, 31, 82, 331, 338, 342
- i**
- ibuprofen 17, 83, 84, 87, 404, 408, 409
 - idarubicin 372
 - ifosphamide 365, 366
 - iloperidone 309
 - imatinib 214, 373, 374, 596
 - imidazoline clonidine 338
 - imidazopyridines 310
 - imipenem 384, 385, 387
 - imipramine 69, 302, 303, 405, 411, 412, 507

indapamide 345, 346
 indinavir 82, 84, 86, 88, 596
 inflammatory bowel disease (IBD) 19, 208, 268, 623
 insecticides 267, 685
 – carbamate insecticides 686, 687
 – carboxylesterases, detoxification by 165, 168, 175–177
 – drug-insecticide interactions 175
 – metabolism of 688, 690
 – – extrahepatic 693, 694
 – – factors affecting 694–697
 – – phase I hepatic 688–692, 689, 691
 – – phase II hepatic 692, 693
 – organochlorine insecticides 674, 688
 – organophosphate insecticides 685, 686, 686
 – PONs, detoxification by 184
 – pyrethroid insecticides 686, 687
 interferon 84, 396, 397
 intestines
 – drug transport into 211, 212, 213
 – flavonoid metabolism 547–549
 4-iodo-2,5-dimethoxyamphetamine (DOI) 430, 438, 439
 iodothyronines 121, 125, 126, 135
 irbesartan 335, 335
 irinotecan 79, 214, 289, 290, 295, 371
 – and carboxylesterases 173
 – – drug transporter-carboxylesterase interaction 175
 – – UGT-carboxylesterase interaction 174, 175
 – and Gilbert–Meulengracht syndrome 83, 85, 86
 – toxicity 83, 84, 85, 86
 – and UGT polymorphisms 88, 269
 isoflavones 545, 546, 551, 553, 563, 568
 isoniazid 48, 177, 260, 396, 507, 509
 isoniazide 17
 isoprenaline 19
 isorhamnetin 550
 isothiocyanates 625, 626
 itraconazole 310, 336, 386, 388, 389

k

kaempferol 555, 559, 562, 564, 567, 624
 – regulation of CYPs 569, 624
 ketamine 267, 405, 414, 443
 ketobemidone 406, 418
 ketoconazole 51, 228, 479, 527, 618, 619
 ketoprofen 83, 84, 87, 404, 409
 ketorolac 404, 409

kidneys
 – drug transport into 211, 213, 214
 – elimination of lipophilic chemicals 287
 kinases 532, 556, 557

l

l- α -acetylmethadol (LAAM) 406, 418
 l-DOPA 18, 314
 lactoperoxidase 9
 lamivudine 390
 lamotrigine 311, 312
 lead and lead compounds 654, 655
 letrozole 373, 619
 leukotoxin 179
 levetiracetam 311, 312
 levomepromazine 307
 levorphanol 406, 418
 ligand regulation of CYPs 229, 230
 lindane 655
 lipases 189, 190
 liposomal amphotericin B 386
 lipoxygenases (LOXs) 559–562, 614, 621
 lisinopril 332
 liver
 – biotransformation 290
 – drug transport into 211, 213
 – flavonoid metabolism 547–550
 liver X receptor (LXR) 97, 100, 185, 273, 616, 627
 – regulation of CYPs 235, 238, 530
 lofepramine 302
 loperamide 407, 418, 419
 lopinavir 393, 394, 394, 395
 lorazepam 367, 507
 losartan 266, 335, 335–337, 336
 lovastatin 3, 183, 234, 289, 356, 532, 532, 534
 luteolin 557, 559, 561–563, 567, 624
 lysergide (LSD) 430, 432, 434
 lysophosphatidylinositol 188

m

malathion 171, 686, 686, 688, 689, 692
 mannitol 344, 345
 MAO-B inhibitors 314
 maprotiline 302
 melanin 19
 melatonin 311
 meloxicam 404, 409
 melphalan 366
 memantine 313
 membrane transport proteins 199, 200
 menthol 479, 480

- mepacrine 507
 meperidine 176
 mephedrone 431, 442, 442
 mephenytoin 235, 310, 312, 336, 508, 591, 597
 5-mephenytoin 223, 266, 312
 meprobamate 506
 6-mercaptopurine 12, 12, 19, 268, 369, 370
 mercury compounds 655, 656
 meropenem 384, 385, 387
 metamizole 267
 metaproterenol 339
 methadone 267, 419, 507, 509
 methamphetamine 430, 432, 434
 methazolamide 188, 344, 345
 methiocarb 691, 692
 methotrexate 214, 215, 273, 367, 368
 methoxsalen 469, 479
 4'-methoxy- α -pyrrolidinopropiophenone (MOPPP) 431, 447, 447, 448
 5-methoxy-diisopropyl-tryptamine (5-MeO-DIPT) 431, 450, 450
p-methoxyamphetamine (PMA) 430, 437, 438
 methoxychlor 674, 676, 677
p-methoxymethamphetamine (PMMA) 430, 438
 1-(4-methoxyphenyl)piperazine (MeOPP) 431, 445, 446
 8-methoxypsoralen 533, 534, 534
 4'-methyl- α -pyrrolidinobutyrophenone (MPBP) 431, 447, 449
 4'-methyl- α -pyrrolidinohexanophenone (MPHP) 431, 447, 448, 449
 4'-methyl- α -pyrrolidinopropiophenone (MPPP) 431, 447, 448
 4'-methyl- α -pyrrolidinovalerophenone (PVP) 431, 447, 449
N-methylbenzodioxolyl butanamine (MBDB) 430, 436, 436–438
 3-methylcholanthrene 99, 151, 177, 232, 233
 methyl dopa 18, 19, 338, 338
 methylenedioxy- α -pyrrolidinopropiophenone (MDPPP) 431, 447, 447, 448
 4-methylenedioxyamphetamine (MDA) 430, 436, 436–438
 methylenedioxyamphetamines 430, 435–437, 436
 1-(3,4-methylenedioxybenzyl)piperazine (MDBP) 431, 445, 445
 3,4-methylenedioxyethylamphetamine (MDEA) 430, 436, 436–438
 3,4-methylenedioxyamphetamine (MDMA) 267, 430, 436, 436–438
 3',4'-methylenedioxypropylvalerone (MDPV) 431, 447, 449, 450
 methylhydrazines 367
 methylone 431, 441, 442, 442
 methylphenidate (MPH) 173, 311
p-methylthioamphetamine (4-MTA) 430, 438
 methyltransferases 18, 19
 metolazone 345
 metoprolol 339, 343
 metronidazole 507
 metyrapone 479
 mianserin 302, 303
 micafungin 386, 388
 mice 99, 100
 microsomal ethanol oxidizing system (MEOS) 495, 498, 503, 504–510
 midazolam 226, 293, 310, 592, 597–599, 619, 622
 milnacipran 305
 minaprine 305
 minoxidil 133
 miRNAs 270, 272, 273
 mirtazapine 302, 303
 mitomycin C 13
 mitoxantrone 9, 556
 moclobemide 306
 moexipril 332
 molybdoenzymes 11, 12, 12, 19
 mono-nitrogen oxides (NO_x) 656
 monoamine oxidase (MAO) 11, 49, 367, 434, 587
 mood stabilizers 311–313
 morin 555, 559, 560, 562, 569, 624
 morphine 532, 533, 535
 – as drug of abuse 430, 432, 432
 – as painkiller 406, 407, 416, 419
 – synthesis from codeine 266, 290, 292, 416, 417
 – synthesis from heroin 417, 418
 – synthesis from nicomorphine 419
 multidrug resistance proteins (MRPs) 354
 – carboxylesterases, interaction with 175
 – as drug transporters 208, 213, 214, 337, 357
 – and flavonoids 547, 555, 556
 mycophenolic acid 597
 myeloperoxidase 9
 myricetin 556, 557, 559, 562, 565, 567, 569, 624
 myristicin 533, 535

n

N-acetyl-*p*-benzosemiquinoneimine (NAPQI) 6, 18, 290, 407
 – formation of 5, 7, 8, 290
N-acetyltransferases (NATs) 17, 18, 49, 134, 260, 263, 570
 – and environmental pollutants 643, 644, 647
 – polymorphisms 292, 396
 Na⁺–K⁺–2Cl[–] symport inhibitors 345, 346
 NADPH oxidase 13
 NAD(P)H oxidoreductase 13, 14
 NADPH-P450 reductase 28, 37, 38, 41, 41, 50
 nalbuphine 416, 419
 naphthodianthrones 588, 589
 α-naphthoflavone 40, 46, 561, 569
 β-naphthoflavone 177, 232, 559, 569, 570, 572
 naphthol structures 88
 naphtoflavone 624
 naproxen 404, 408, 409, 410
 naringenin 551, 554, 556, 571, 572, 622, 623, 628
 naringin 565, 622, 623, 623, 624
 natural product chemicals 519, 536
 – classes 521, 522
 – considerations with use as drugs 520, 521
 – drug-drug interactions 520, 521
 – flavonoids, *see* flavonoids
 – food components/supplements, *see* food components/supplements
 – metabolism of 521
 – plant products as drugs 520
 – polyketides, shikimates, alkaloids 531, 532
 – – biotransformation 532, 532, 533, 534, 534–536
 – St John's Wort, *see* St John's Wort (*Hypericum perforatum* L.)
 – terpenoids, *see* terpenoids
 nebiivolol 343
 nefazodone 305, 444, 446
 neuraminidase inhibitors 391
 nevirapine 234, 267, 393
 nicomorphine 419, 420
 nicotine 11, 18, 267, 296, 465, 483, 533, 535
 – absorption 465, 466
 – distribution in body tissues 466
 – excretion 466, 468
 – factors affecting metabolism 477
 – – age 478
 – – gender and pregnancy 477, 478

– – genetics 471, 472–475, 476, 477
 – – meals and chronopharmacokinetics 479
 – – menthol 480
 – – other factors 480
 – – smoking 480
 – – xenobiotics 479
 – implications in metabolism variation and CYP2A6 activity
 – – health consequences of smoking 481
 – – smoking behaviors 481
 – – smoking cessation outcomes 482
 – metabolism of 233, 234
 – – pathways 468
 – – primary metabolites 468–470
 – – secondary metabolites 470
 – – tertiary metabolite 470
 – pharmacokinetics 467
 nifedipine 226, 235, 349, 599
 nilotinib 374
 nitrenium 17, 18, 570, 643, 644
 nitric oxide synthases 37
 nitrogen dioxide 641, 656
 nitrogen oxide 641, 656
p-nitrophenylacetate 176, 190
 nitrosamines 7, 470, 481, 483, 507, 509, 614, 656
 nomenclature
 – of CYPs 29, 29, 30, 275
 – of GSTs 148–151, 152, 153
 – of SULTs 118
 – of *UGT1A* 70, 71
 nonalcoholic fatty liver disease (NAFLD) 294, 505
 nonsteroidal anti-inflammatory drugs (NSAIDs) 266, 267, 404, 408–410
 noradrenaline 17, 18
 norafloxacin 507
 norharman 533, 535
 nortriptyline 302, 405, 410, 411
 nuclear factor erythroid 2-related factor 2 (Nrf2) 16, 96, 98
 nuclear receptors 175, 212
 – regulation of CYPs 97, 227–229, 235
 – *see also specific receptor*
 nutraceuticals 565–568, 573

o

olanzapine 308, 507
 omeprazole 225, 235, 266, 599
 opioids 416–421
 opipramol 303
 oral contraceptives 51, 125, 477, 478, 599, 600

- organochlorine insecticides 237, 674, 688
 - PCBs 677, 678
 - organophosphate insecticides 171, 175, 685, 686, 686
 - extrahepatic metabolism 693, 694
 - interaction with xenobiotics 695
 - phase I metabolism 688, 689, 689, 690, 690, 691, 691, 692
 - phase II metabolism 692, 693
 - protection from, by carboxylesterases 165, 168, 175
 - variability in metabolism 696, 697
 - oseltamivir 169, 170, 171, 176, 391
 - osmotic diuretics 344, 345
 - oxaliplatin 367, 368
 - oxazaphosphorine 365, 366
 - oxazepam 15, 310
 - oxcarbazepine 311, 312
 - oxidative stress
 - and CYPs 47, 48
 - and ethanol metabolism 504, 508
 - and flavonoids 545
 - and GSTs 150, 155
 - and Nrf2 98
 - and PONs 185, 188
 - oxycodone 407, 416, 420
 - oxymorphone 407, 416, 420
 - ozone 641, 656
- p**
- p*-substituted amphetamines 430, 436, 437, 438
 - paclitaxel 213, 214, 237, 370, 371, 528, 529, 572
 - painkillers 403
 - acute pain
 - cyclooxygenase-2 selective inhibitors 410
 - dexmedetomidine 403
 - nonsteroidal anti-inflammatory drugs 408–410
 - paracetamol 407
 - chronic pain
 - antiepileptics 415
 - ketamine 414
 - opioids 416–421
 - SNRIs 412, 413
 - SSRIs 413, 414
 - tricyclic antidepressants 410–412
 - various other drugs 415, 416
 - enzymes used 404–407
 - paliperidone 308, 309
 - pancreatic cancer 94, 95
 - pantoprazole 266
 - paracetamol (acetaminophen) 15, 16, 404, 407, 507, 507, 509
 - age effects 293
 - biotransformation 290
 - flavonoid interaction 572
 - gender effects 293
 - metabolism pathways 5, 6
 - NAPQI, formation of reactive 5, 7, 8, 290
 - paraoxonases (PONs) 183, 184, 289, 290
 - catalytic mechanism 185, 186, 187
 - classification and structure 184, 185
 - comparison of PONs 187
 - inhibition of 187, 188
 - polymorphisms 696
 - role in metabolism
 - of cardiovascular drugs 334, 352, 353, 353, 355, 357
 - of insecticides 690, 692, 693, 696
 - substrates 183
 - parathion 618, 656, 657, 685, 688, 689, 689, 691
 - parecoxib 405, 410
 - pargyline 306
 - paroxetine 305, 405, 414
 - pazopanib 374
 - penicillins 383–386
 - pentanol 504, 507
 - pentazocine 420
 - pentobarbital 506
 - pentopril 332
 - peptidases 190
 - peramivir 391
 - perazine 307
 - perindopril 332
 - permethrin 687, 688
 - peroxidases 8, 8, 9, 18, 150
 - peroxisome proliferator-activated receptor (PPAR)- α system 100, 185, 500, 616, 627, 657
 - regulation of CYPs 33, 227, 232, 271
 - perphenazine 307
 - pethidine 407, 420
 - pharmacogenetics 4, 259
 - of antimicrobial agents 393, 394, 394, 395, 396, 397
 - of carboxylesterases 172, 173
 - of COMT 19
 - of FMOs 11
 - genetic polymorphisms, *see* genetic polymorphisms
 - of Gilbert–Meulengracht syndrome 83
 - of NATs 17, 18
 - nicotine clearance and metabolism 471, 472–475, 476, 477
 - of SULTs 132, 133

- of TPMT 19
- of UGTs 16, 68
- websites 264, 265
- *see also* pharmacogenomics
- pharmacogenomics 259, 260
- of carboxylesterases 172–175
- drug metabolism phenotype 270
- – epigenetic influences 272, 273
- – polygenic inheritance 270, 271
- of drug transporters 215, 269, 270
- genetic polymorphisms, *see* genetic polymorphisms
- technologies and applications 273, 274
- – genetical genomics 275, 276
- – GWAS 274, 275
- websites 264, 265
- *see also* pharmacogenetics
- pharmacokinetics
- defined 3
- and drug transporters 212–214
- gender effects 292, 293
- phenacetin 591
- phenanthrene 612
- phencyclidine derivatives 443, 443, 444
- phencyclidine-derived designer drugs 431, 443, 443, 444
- phencyclidine (PCP) 432, 434, 435
- phenelzine 306
- phenethylamines (2Cs) 430, 439, 439–441
- phenobarbital 48, 51, 177, 311, 479
- induction of CYPs 226, 234, 235, 479
- phenothiazine 306
- phenothiazines 306, 507
- phenylalkylamines 349
- phenylbutazone 507
- N*-(1-phenylcyclohexyl)-2-ethoxyethanamine (PCEEA) 431, 443, 444
- N*-(1-phenylcyclohexyl)-2-methoxyethanamine (PCMEA) 431, 443, 444
- N*-(1-phenylcyclohexyl)-3-ethoxypropylamine (PCEPA) 431, 443, 443
- N*-(1-phenylcyclohexyl)-3-methoxypropanamine (PCMPA) 431, 443, 443
- N*-(1-phenylcyclohexyl)propanamine (PCPr) 431, 443, 443
- phenylene-chlorobenzenesulfonamide 172, 172
- phenylephrine 337, 337
- phenylmethylsulfonyl fluoride (PMSF) 171
- phenytoin 179, 226, 234, 266, 312, 366, 367, 507, 507
- phloroglucinols 588
- phorate 691, 692
- 3'-phosphoadenosine-5'-phosphosulfate (PAPS) 6, 117–119, 119, 121, 128
- synthesis of 119, 120
- phthalates 33, 226, 657, 674
- pilocarpine 479, 533, 535
- pimozide 307
- piperacillin 384, 385
- piperacilline 387
- piperazines 431, 444–446, 445
- piritramide 420
- pitavastatin 185, 356
- pivalopril 332
- platinum-containing agents 200, 215, 367
- polyamine oxidase (PAO) 11
- polychlorinated biphenyls (PCBs) 126, 134, 658, 677, 678
- polychlorinated dioxins 658, 659
- polychlorinated furans 658, 659
- polycyclic aromatic amines (PAAs) 611–613
- polycyclic aromatic hydrocarbons (PAHs) 125, 126, 134, 225, 612, 613, 657, 658, 674
- polyenes 386, 389
- polyhalogenated aromatic hydrocarbons (PHAHs) 126, 134, 135
- polyketides 531, 532, 532, 534–536
- polymorphisms, *see* genetic polymorphisms
- posaconazole 386, 388, 389
- prasugrel 169, 170, 173, 174
- pravastatin 185, 356, 600
- prazosin 339, 340, 340, 341, 344
- prebiotics 611, 628, 629
- prednisone 600
- pregabalin 312, 415
- pregnane X receptor (PXR)
- activation with other receptors 228, 229
- and environmental estrogens 677, 678
- heterodimer with RXR- α 226, 616
- and insecticides 175
- miRNA control of 34, 273
- nicotine metabolism 479
- regulation of CYPs 33, 226, 234, 292
- – CYP2B6 234, 235
- – CYP2C subfamily 236
- – CYP3A subfamily 237, 238, 620
- regulation of UGTs 97, 100
- and St John's Wort 521, 591, 592
- and terpenoids 528
- pregnenolone 126, 529
- pregnenolone 16 α -carbonitrile 177, 677
- primaquine 260, 396
- probiotics 611, 622, 628, 629
- procainamide 9, 166, 169
- procaine 169, 176

- procarbazine 367, 507
 profenofos 686, 686, 688
 progesterone receptor (PR) 231
 propofol 69, 267
 propoxyphene 508
 propranolol 11, 342, 343, 344, 507
 prostaglandin H synthase (COX) 6, 8, 8, 9, 18, 559–562, 621
 prostaglandins 8, 31, 147, 149, 233, 561, 621
 protease inhibitor therapy 86
 proteases 190
 proteasome inhibitor 374
 protein 620, 621
 prothiophos 692
 proton pump inhibitors (PPI) 266
 prulifloxacin 183, 184
 pseudohypericin 306, 587–589, 590
 psychostimulants 311
 pulegone 522, 525, 526, 526
 purine analogs 369, 370
 pyrethroid insecticides 175–177, 686
 – extrahepatic metabolism 693
 – interaction with xenobiotics 695
 – phase I metabolism 687–690, 692
 – phase II metabolism 693
 – protection from, by carboxylesterases 165, 175
 pyrimidine analogs 368
 pyrrolidinophenones 431, 446–450, 447
 α -pyrrolidinopropiophenone (PPP) 431, 447, 447
 pyrrolones 310
 pyrrolysates 507, 570
- q**
- quazepam 310, 601
 quercetin 589, 590, 591, 591
 – and AhR 559
 – and ATP-binding proteins 555–557
 – bioavailability 546, 547
 – and carcinogens 569, 570
 – cytoprotection 567
 – cytotoxicity 567
 – drug-flavonoid interactions 572, 625
 – elimination 553
 – excretion 550
 – health issues 563
 – metabolism 548–550
 – and plasma proteins 554, 555
 – redox enzyme activity modulation 561, 562
 – regulation of CYPs 624
 – SULT inhibition 17
- quetiapine 309
 quinacrine 507
 quinapril 332
 quinine 438, 532, 533, 535
- r**
- rac-methadone 407
 raltegravir 392, 393
 ramipril 332, 333, 333, 334, 334
 rasagiline 314
 reactive oxygen species (ROS)
 – and arsenic compounds 645
 – and CYPs 48, 232
 – and environmental estrogens 677
 – and ethanol metabolism 493, 498, 499, 500, 504, 505, 506
 – and flavonoids 559–563, 566, 567
 – and FMOs 10
 – and GSTs 150
 – and NADPH oxidase 13
 reboxetine 305
 reductases 14, 15
 remifentanyl 417
 renin–angiotensin–aldosterone system (RAAS) 331, 332, 332
 – drugs targeting
 – ACE inhibitors 332–334, 333, 334
 – ARBs 334–337, 335, 336
 repaglinide 16
 resmethrin 687
 respiratory viruses 391
 resveratrol 225, 233, 533, 535, 557, 613
 retinoic acid 233, 616–618, 617
 – and ethanol metabolism 501, 502, 502, 506, 507, 508, 509, 510
 – and terpinoid metabolism 525, 530, 531
 retinoic acid receptor (RAR) 227, 229, 232, 616
 retinoic X receptor (RXR)- α 229, 612, 616
 – heterodimer with CAR 33, 226, 237
 – heterodimer with PPAR- α 33, 232
 – heterodimer with PXR 33, 226, 237, 619
 – heterodimer with VDR 237
 – upregulation by GR 228, 235, 236
 retinol 499, 616–618, 617
 – and ethanol metabolism 501, 502, 502, 506, 507, 509, 510
 – and terpinoid metabolism 530, 531
 RH1 13
 ribavirin 83, 84, 390, 391, 396, 397
 riboflavin 620
 riddelliine 532, 533, 535
 rifampicin 51, 267, 388, 507
 – CYP induction 236, 479

- PXR activation 226, 228, 235
 - rimiterol 19
 - risperidone 308, 309
 - ritodrine 339
 - ritonavir 234, 295, 392, 394, 394, 395
 - rivastigmine 313
 - rosuvastatin 266, 356
 - route of administration 3
 - rufinamide 169
 - rutin 546, 559, 566, 570, 589, 590, 625
- S**
- safrole 17, 133, 533, 534, 535
 - salbutamol 9
 - selective estrogen receptor modulator (tamoxifen) 266, 289, 372, 373
 - selective serotonin reuptake inhibitors (SSRIs) 199, 302–305, 304, 405, 410, 413, 414
 - selegiline 314, 479
 - senecionine 532, 533, 535
 - serotonin 11, 17, 444, 445
 - serotonin-norepinephrine reuptake inhibitors (SNRIs) 302, 405, 410, 412, 413
 - serotonin transporter protein SERT 199
 - sertindole 309
 - sertraline 305
 - sex, influence on drug metabolism 292, 293
 - shikimates 531, 532, 532, 533, 534, 534, 535, 536
 - short-chain dehydrogenase/reductases (SDRs) 14, 15
 - silencing mediator for retinoic acid and thyroid hormone receptors (SMRT) 229, 232, 238
 - simvastatin 79, 83, 84, 185, 234, 289, 356, 601
 - smoking 295, 296, 348, 465, 480, 483, 643
 - *see also* nicotine
 - soman 170, 696
 - sorafenib 374
 - sorivudine 14
 - spirapril 332
 - spironolactone 166, 169, 348, 349
 - splice variant regulation 98, 99
 - squalene 522, 524, 529, 530
 - St John's Wort (*Hypericum perforatum* L.) 306
 - antidepressive activity 587, 588
 - chemical constituents 583, 584, 585, 586
 - commercially available extracts 586
 - drug interactions 51, 521, 571
 - *in vitro* studies 591, 591, 592
 - *in vivo* studies 592, 593–602
 - name, history of 583
 - pharmacokinetics
 - flavonoids 589
 - hyperforin 588
 - hypericin 589
 - naphthodianthrones 588, 589
 - phloroglucinols 588
 - pseudohypericin 590
 - quercetin 590
 - rutin 590
 - statins 185, 267, 289, 355, 356, 357, 357
 - steroid receptors 227–230
 - sterols 30, 30, 31, 117, 126
 - streptozotocin 177
 - styrene and styrene oxide 659
 - sufentanil 417
 - sulfation 117–119, 119, 133, 135
 - sulfonamides 9, 18, 313, 396, 507
 - sulfonylureas 507
 - sulfotransferases (SULTs) 16, 17, 117–119, 134
 - assays for SULT activity 128
 - bioactivation and toxicology 133–135
 - flavonoid interaction 17, 548, 561, 569, 572
 - future research 135
 - inhibition of 17
 - nomenclature 118
 - pharmacogenetics 132, 133
 - polymorphisms 117, 118, 132
 - reaction 119
 - research history 118, 119
 - role in metabolism
 - of environmental pollutants 644
 - of estrogens 677
 - of flavonoids 549
 - of insecticides 693
 - of natural products 533, 535
 - of painkillers 404, 407
 - structure and function 128–132
 - key elements of SULT active site 131
 - SULT enzyme family 121
 - human SULTs and their substrates 124
 - inter-relationships 122, 123
 - sequence alignment 122
 - SULT1 family 121, 124–126
 - SULT2 family 126
 - SULT3, 4, 5 and 6 families 127
 - sulfur dioxide 641, 642, 659
 - sulpiride 309
 - sulprofos 691, 692
 - sumatriptan 313
 - sunitinib 374

t

- tacrolimus 223, **601**
- tamoxifen 11, 266, 290, 295, 372, 373, **507**, 571, 674
- tapentadol 415, 416
- taxanes 370–371
- tazobactam 384, 385, 387
- tegafur 368
- telaprevir 390
- telbivudine 390
- telmisartan 335
- teniposide 372
- tenofovir 390
- terazosin **340**
- terbutaline 9
- terfenadin 623, 624, 629
- terfenadine 51, 269, 622
- terpenoids
- biosynthesis 522, 523, 524, 525
 - biotransformation
 - – diterpenoids 528
 - – monoperpenoids 524–527
 - – monoterpenoids 526
 - – sesquiterpenoids 527, 528
 - – triterpenoids 525, 528–531
- testosterone 126, 147, 501, 529, 568, **591**
- tetrachloroethylene 660
- Δ^9 -tetrahydrocannabinol (THC) **430**, 432, 433, 528
- tetramethrin 687
- theophylline **507**, **601**, 623
- thiamine 620
- thiazide/thiazide-like diuretics 345, **346**, 347
- 6-thioguanine 12, 19, 268, 369, 370
- 6-thiopurine analogs 369, 370
- thiopurine S-methyl transferase (TPMT) 12, 18, 19, 268, 292, 369
- thioridazine 307
- thiotepa 366, 444
- thioxanthenes 306
- thrombosis 331, 352, 353
- thyroid receptor (TR) 227, 229, 232, 616
- tiagabine 311, 312
- tilidine **407**, 416, 420
- tobramycin 380, 381
- tolazoline **507**
- tolbutamide 37, 266, **507**, 507, 592, **601**, 617
- tolcapone 314
- topiramate 312
- topotecan 371
- toremide 345, **346**
- toxic metabolites 287, 290, 509, 694
- tramadol **407**, 416, 421
- tranquilizers and hypnotic agents 309, 310, **507**
- transcriptional regulation
- of CYPs 32, 32–34
 - of *UGT1A* genes 70, 95, 96, 98, 101
- transcriptional regulation of human CYPs 224, 225
- factors affecting CYPs 223
 - – environmental factors 224
 - – genetic polymorphism 223, 224
 - – physiological and pathophysiological factors 224
 - ligands 229, 230
 - regulation of CYPs
 - – CYP1A subfamily 230–232
 - – CYP1B1 232, 233
 - – CYP2A6 233, 234
 - – CYP2B6 234, 235
 - – CYP2C subfamily 235, 236
 - – CYP3A subfamily 236–238
 - steroid and nuclear receptors 227
 - transcriptional mechanisms
 - – coactivator sharing 229
 - – direct binding to gene promoter 227
 - – indirect binding to gene promoter 227
 - – ligand sharing 228
 - – metabolic cross-talk 229
 - – receptor cascade 228
 - – receptor cross-talk 228
 - – regulating the regulator 228
 - – response element sharing 228
 - xenoreceptors 225
 - – aryl hydrocarbon receptor (AhR) 225, 226
 - – constitutive androstane receptor (CAR) 226, 227
 - – pregnane X receptor (PXR) 226
- transporting systems 199
- drug transporters, *see* drug transporters
- tranlycypromine 306, 479
- triamterole 347, 347, 348, 348
- triazine herbicides 676
- triazolam 310
- trichothecenes 615
- tricyclic antidepressants 302, 303, 410–412
- trifluoromethyl ketone (TFK)-containing compounds 171, 172
- 1-(3-trifluoromethylphenyl)piperazine (TFMPP) **431**, 445, 446
- 2,4,5-trimethoxyamphetamine (TMA-2) **430**, 438, 439
- trimipramine 302

tryptamine 429, 479
 tryptamine-derived designer drugs 431
 tryptamines 450, 450
 tyrosine kinase inhibitors 87, 88, 373, 374

u

UDP-glucuronosyltransferases (UGTs) 15, 16, 67
 – carboxylesterases, interaction with 174, 175
 – gene organization 68
 – glucuronidation 69
 – pharmacogenetics 16, 68
 – polymorphisms 71, 269, 292, 477
 – PXR regulation of 97, 100
 – *UGT1A* supergene family, *see UGT1A* supergene family
 – websites 15
UGT1A supergene family
 – animal models for study 99, 100
 – and antiretroviral protease inhibitor therapy 86
 – bilirubin glucuronidation 78, 79
 – and cancer 89–92
 – – breast cancer 87
 – – colorectal cancer (CRC) 80, 85, 87, 93
 – future research 100, 101
 – gene locus 68–70, 70
 – human locus 70, 71
 – hyperbilirubinemia 71, 77, 78–80
 – nomenclature 70, 71
 – regulation of 96
 – – by AhR/ARNT complex 95, 96, 96, 98
 – – by FXR 97, 98
 – – by HNFs 96, 97
 – – by Nrf2 98
 – – by splice variants 98, 99
 – – transcriptional regulation 95
 – – by XREs 70, 95, 96, 96, 98
 – sequence variability 71
 – – *UGT1A1* gene 72, 73, 78–80
 – – *UGT1A3* gene 74, 75
 – – *UGT1A7* gene 76
 – *UGT1A* variants and disease association studies 89–92
 – *UGT1A1* gene
 – – advantage/risk associated with variability 80, 80, 81, 82
 – – and antiretroviral protease inhibitor therapy 86
 – – bilirubin glucuronidation, importance in 78, 79
 – – and cancer 82, 83, 86, 87

– – and cardiovascular disease 82
 – – and drug toxicity 83, 85, 86
 – – sequence variability 72, 73, 78–80
 – *UGT1A3* gene 74, 75, 86–88
 – *UGT1A7* gene 88, 93
 – – age effects 93, 94
 – – and antiretroviral protease inhibitor therapy 86
 – – and cancer 93–95
 – – irinotecan toxicity 85, 86
 – – sequence variability 76
 urea 344, 345
 uric acid 12, 500, 562

v

valacyclovir 189, 190, 390
 valacyclovirase 190, 191
 valgancyclovir 390
 valproate (VPA) 228, 312, 406, 415
 valproic acid 226, 227, 234, 237, 266
 vancomycin 382, 383
 venlafaxine 305, 405, 412, 413
 verapamil 188, 269, 289, 295, 349–351, 350, 351, 601, 602
 VID400 619
 vigabatrin 311, 312
 vinca alkaloids 214, 370
 vincristine 370
 vinyl chloride 507, 660
 vitamin A 522, 530, 531, 616–618, 617
 vitamin D 50, 87, 522, 524, 529, 530, 618, 619, 654
 vitamin D receptor (VDR) 97, 227, 235–237, 273, 530
 vitamin E 226, 237, 619
 vitamin K 226, 352
 vitamin K antagonists 352
 vitamins 30, 31, 611, 612, 616–620, 617
 voriconazole 386, 388, 389, 602
 vorinostat 373

w

warfarin 293, 352, 354, 602, 617
 – and CYPs 37, 235, 266, 267, 507, 507, 620
 websites
 – CYP alleles 36, 471, 476
 – CYPs 29
 – dosage adaptation in CRRT 384
 – drug interactions 392
 – drug transporters 200
 – European Committee on Antimicrobial Susceptibility Testing 385

- pharmacogenetics 264, 265, 396, 397
 - receptor cross-talk 228
 - UGT alleles 15
 - Widmark equation 496, 497
- x**
- xanthine oxidase (XO) 10–12, 12, 369, 498, 559–562
 - xenobiotic-responsive elements (XREs) 95
 - regulation of CYPs 225, 231–233, 235, 236
 - regulation of GSTs 151, 558
 - regulation of *UGT1A* genes 70, 95, 96, 96, 98
 - xenobiotic transformation, *see* drug metabolism
 - xenoreceptors 227, 228, 229
 - aryl hydrocarbon receptor (AhR) 225, 226
 - constitutive androstane receptor (CAR) 226, 227, 237
 - pregnane X receptor (PXR) 226, 237
- y**
- yohimbine 340, 341, 342
- z**
- zaleplon 310
 - zanamivir 391
 - zidovudine 16, 190
 - ziprasidone 309
 - zofenopril 332
 - zolpidem 310
 - zonisamide 312
 - zopiclone 310
 - zotepine 309
 - zuclopenthixol 307