

Index

a

- abacavir 369f.
 ABT, *see* 1-aminobenzotriazole
 acetaminophen 71, 273ff.
 – metabolic activation 73
 – metabolism 72
 acetaminophen-like metabolite 276
 N-acetyl-*p*-benzoquinone imine (NAPQI)
 5, 73
 N-acetylcysteine 275
 N-acetyltransferase (NAT) 16, 283
 N-acetyltransferase-2 (NAT-2) 79, 283
 acute liver failure (ALF) 363
 acylating agent 320
 afatinib 319
 affinity label 313
 aflatoxin 214
 aflatoxin B₁ (AFB₁) 2
 – bioactivation 215
 AKT inhibitor, *see* protein kinase B inhibitor
 alanine transaminase (ALT) 363
 alclofenac
 – metabolic activation 119
 aldehyde oxidase 60
 alendronic acid 290
 alkaloid
 – pyrrolizidine 210
 alkene
 – terminal 117f.
 3-alkyl pyrrole 112
 – activation 112
 alkylating species 173
 2-alkylimidazole 57
 3-alkylindole analogue 113
 3-alkylindole derivative 112
 alkylpiperazine 258
 alkyne 56f.
 – bioactivation 119f.
 – internal 120
 – terminal 117ff.
 allele association
 – HLA 370
 allopurinol 373
 2-allylisopropylacetamide (AIA) 117f.
 alpidem 304f., 336, 349
 amanitin 204
 Ames assay 29
 AMG 458 139ff.
 α-amidoacetonitrile 324
 amine 49
 – aromatic, *see* aromatic amine
 – carcinogenicity of aromatic and
 heteroaromatic amine 13
 – drug–drug interaction 51
 amineptine 196, 342ff.
 2-amino-3,8-dimethylimidazo[4,5-*f*]
 quinoxaline (MeIQx) 216
 – bioactivation 218
 2-amino-1-methyl-6-phenylimidazo[4,5-*b*]
 pyridine (PhIP) 216
 – bioactivation 218
 aminoazo dye 15
 1-aminobenzotriazole (ABT) 58f.
 aminoglutethimide 188
 5-aminooxindole 253
 – derivative 254
 ortho-aminophenol 101
 para-aminophenol 101
 2-aminothiazole 109
 amitriptyline 282ff., 343f.
 – metabolism 287
 amlodipine 274
 amodiaquine 252
 – metabolic activation 101
 amoxicillin 132, 273ff., 288
 angiotensin converting enzyme
 inhibitor 294ff.
 angiotensin II receptor antagonist 298

anilide structural alert 299
 aniline 98, 188
 – metabolic activation 100
 aniline cancer 15
 animal
 – plant–animal warfare 204
 anthracycline 157ff.
 – antibiotic 158
 – bioreductive activation 173
 anthramycin 318
 anti-HIV drug 108
 anti-anxiolytic drug 253
 antibiotic 131, 158, 170, 281f., 297ff.
 antibody 8
 anticancer drug 21, 160
 – quinone-containing 21
 antidepressant drug 253, 293, 344
 antidiabetic agent 274, 282ff., 349
 antihypertensive drug 297f.
 antimalarial agent 252
 antipain 322ff.
 antipsychotic 368
 aplaviroc 366
 ar-tumerone 318
 aripiprazole 343f.
Aristolochia 208
 aristolochic acid 208
 – bioactivation 209
 – metabolism 209
 aromatic amine 98ff.
 – carcinogenicity 13
 – metabolic activation 100
 aromatic carboxamide
 derivative 35
 aromatic ring
 – electron-rich 251
 artemisinin 166
 – bioactivation 167
 – derivative 166
 arylindenopyrimidine derivative
 – pyrrolidine-substituted 34
 aspartate transaminase (AST) 363
 aspirin 322f.
 atenolol 187
 atorvastatin 273
 – metabolism 276
 ATPase
 – gastric 278
 augmentin 288
 azaheterocyclic compound
 – polycyclic 216
 aziridinylbenzoquinone 170ff.
 – metabolic activation 172
 azithromycin 274

b

benazepril 294ff.
 benzbromarone 373
 1,3-benzodioxole motif 115f.
 – metabolic activation 117
 benzene oxide 4
 benzo[a]pyrene 2
 benzodiazepine drug 297ff.
 1,3-benzodioxole structural alert 292
 benzoquinone 170
 – *ortho*-(1,2)-benzoquinone (BQ) 4
 – *para*-(1,4)-benzoquinone (BQ) 4
 BIBW2992 319
 bile salt export pump (BSEP) inhibition 197,
 288, 348ff.
 bioactivation 203ff.
 – detection 233
 – herbal remedy 205
 biomarker
 – toxicity 369
 bioreduction
 – adical intermediate 157
 black box warning 365
 boceprevir 322ff.
 2-bromo-2-chloro-1,1,1-trifluoroethane,
see halothane
 buprenorphine 300ff., 350
 buspirone 336
cis-2-butene-1,4-dial 23ff.
 BZQ 170

c

calcium channel antagonist 327
 calcium receptor antagonist 36, 347
 calcium sensing receptor (CaSR)
 antagonist 346
 calicheamicin 161
 calicheamicin γ_1 158
 – activation 163
 canertinib 319
 carbamate 320
 carbazilquinone 170
 carboxylic acid 189
 carbutamide 195
 carcinogenesis 1
 carcinogenic substance 14
 carcinogenicity
 – aromatic and heteroaromatic amines 13
 – dihaloalkane 28
 – ethyl carbamate 26
 – furan 23
 – nitrosamine 17
 – quinone 19
 – vinyl halide 26

- carisoprodol 290
 - carvedilol 297
 - cathepsin inhibitor 324
 - cathepsin K inhibitor 324
 - celecoxib 193ff., 290
 - cephalosporin 320
 - chemical reactivity 326ff.
 - experimental approach 326
 - *in silico* approach 328
 - chemokine receptor type 5 (CCR5)
 - antagonist 366
 - inhibitor 365
 - chloramphenicol 188
 - 5-[3-(2-chloroethyl)-1-triazenyl]imidazole-4-carboxamide (MCTIC) 149
 - chlorpropamide 349
 - chymostatin 322ff.
 - ciprofloxacin 297ff.
 - clavulanate 132
 - clavulanic acid 321
 - clinical drug toxicity 359
 - clonazepam 297ff.
 - clopidogrel 151, 273ff.
 - clearance mechanism 281
 - metabolic activation 279
 - clozapine 101, 302ff., 336ff., 368f.
 - metabolic activation 103
 - clozari[®] 369
 - co-trimoxole 282
 - coltsfoot 210
 - comfrey 210
 - concerta 290
 - coniine 204
 - contraindication 367
 - corticotropin-releasing factor-1 (CRF1) receptor antagonist 253
 - pyrazinone-based 256
 - covalent binding
 - reactive metabolite cytotoxicity 5
 - covalent binding assay 231f.
 - covalent inhibitor 313ff.
 - reversible 326
 - covalent modification
 - reversible 322
 - covalent modifier
 - reversible 325
 - CP-671,305 340
 - cyanamide 324
 - cycasin 212f.
 - bioactivation 213
 - cyclobenzaprine 292, 343
 - oxidative metabolism 296
 - cyclooxygenase-2 (COX-2)-selective inhibitor 192ff., 248
 - cyclophosphamide 154f.
 - cysteine protease inhibitor 322ff.
 - cytochrome P450 (CYP) enzyme 1f., 16, 204
 - bioactivation 43ff.
 - inactivator 58
 - inactivation 43ff., 237
 - inhibition 98
 - inhibitor 97
 - mechanism of inactivation 47
 - cytotoxicity
 - reactive metabolite 5
- d**
- dacarbazine 150
 - daily dose trend 270
 - dapsone 188
 - DDI, *see* drug–drug interaction
 - detoxification 6
 - detoxification pathway
 - competing 341
 - diazepam 297ff.
 - diaziquone 170
 - diclofenac 101
 - metabolic activation 102
 - dihaloalkane 28
 - bioactivation 28
 - carcinogenicity 28
 - dipeptidyl peptidase (DPP IV) 324
 - DNA adduct 17
 - DNA alkylation 94, 153
 - nitrogen mustard 96
 - DNA binding 3
 - DNA cleavage 162
 - DNA cross-link formation 212
 - DNA-reactive metabolite
 - bioactivation of vinyl chloride 27
 - bioactivation pathway of nitrosamines 18
 - bioactivation pathway of safrole 22
 - bioactivation pathway of tamoxifen 21
 - donepezil 300ff., 365
 - dose size
 - IADR 342
 - doxorubicin
 - bioreductive activation 173
 - drug
 - bioreductive activation 153
 - nonenzymatically activated 145
 - retrospective analysis of structure–toxicity relationship 185ff.
 - drug design
 - structural alert 225, 336
 - drug discovery 29
 - assay for metabolism-dependent genotoxicity 28

- intrinsically electrophilic compound 131ff.
 - reactive metabolite formation 241
 - reactive metabolite–positive compound 335
 - drug safety data 358
 - drug toxicity
 - rules and laws 363
 - drug withdrawal 360ff.
 - drug–drug interaction (DDI) 46
 - amine-containing drug 51
 - cytochrome P450 time-dependent inhibitor 50
 - drug-induced toxicity
 - reactive metabolite 71ff.
 - drug-metabolizing enzyme
 - bioactivation 43ff.
 - inactivation 43ff.
 - dynemicin 163
 - dynemicin A 158
 - bioactivation 164
- e**
- efavirenz 56, 121
 - elastinal 322ff.
 - electrophile trapping assay
 - qualitative 227
 - quantitative 230
 - electrophilic compound
 - drug discovery 133ff.
 - drug toxicity 135
 - intrinsically 131ff.
 - electrophilic functional group 94
 - electrophilic intermediate
 - bioreductive activation 168
 - enalapril 290ff.
 - enediyne 158ff.
 - cycloaromatization 161
 - 9-membered ring system 160
 - 10-membered ring system 160
 - entacapone 338f.
 - enzyme kinetic principle
 - mechanism-based inactivation 44
 - epidermal growth factor receptor (EGFR) 317
 - covalent EGFR inhibitor 319
 - 1,2-epoxy-3,3,3-trichloropropane (TCPO) 10
 - erlotinib 318
 - escitalopram 274
 - esomeprazole 273ff.
 - esperamicins A₁ 158
 - ester 320
 - estradiol
 - metabolism 20
 - ethinylestradiol 56, 297, 350
 - 17 α -ethinylestradiol 120
 - metabolic activation 301
 - 17 α -ethinylsteroid 120
 - ethyl carbamate 26
 - carcinogenicity 26
 - ezetimibe 302f.
- f**
- fatty acid amide hydrolase (FAAH) 322
 - inhibitor 323
 - felbamate 258ff.
 - fetal hydantoin syndrome 10
 - fluconazole 282ff.
 - 4-fluorofelbamate 258ff.
 - fluoroquinolone antibiotic 297ff.
 - fluoxetine 290
 - FMS inhibitor, *see* tyrosine kinase inhibitor
 - fosamax 290
 - frank electrophile 93
 - furafylline 57
 - furan 23, 55f.
 - carcinogenicity 23
 - metabolic activation 108
 - oxidative bioactivation 24
 - xenobiotic 107
 - furosemide 282ff.
- g**
- gabapentin 290
 - gefitinib 318
 - gemfibrozil 58f.
 - gemtuzumab ozogamicin 165
 - genetic influence
 - reactive metabolite formation 5
 - genotoxicity
 - drug discovery 28
 - reactive metabolite 13ff.
 - germander 205
 - glitazone 191
 - glutathione (GSH) 3, 207, 229f., 249
 - electrophilic compound 134ff.
 - glutathione transferase 28
 - glyburide 282ff., 349
- h**
- halothane 7, 75ff.
 - hepatotoxicity 78
 - metabolism 76
 - oxidative metabolism 77
 - reactive metabolites in immune-mediated toxicity 7
 - reductive metabolism 77
 - helenalin 318
 - heme adduct 48
 - hepatotoxicant 4

- hepatotoxicity 186
 - halothane administration 78
 - herbal remedy 205
 - bioactivation 205
 - herbimycin A 318
 - heteroaromatic amine 13
 - carcinogenicity 13
 - heteroaromatic nitrile 324
 - heteroaromatic ring
 - five-membered 107
 - heterocyclic ring system 242
 - N,N,N',N',N'',N''*-
 - hexamethylmelamine 153ff.
 - human leukocyte antigen (HLA) 370f.
 - hydralazine 60, 79
 - metabolic activation 81
 - metabolism 80
 - hydrazine 105
 - hydrochlorothiazide 294
 - hydrocodone 273
 - 4-hydroxy-1-(3-pyridyl)-1-butanone (HPB) 17
 - 4-hydroxyaniline motif 251
 - para*-hydroxynefazodone 344
 - α -hydroxytamoxifen 22
 - para*-hydroxytrazodone 285
 - hypersensitivity 369
 - hypothemycin 318
- i**
- ibufenac 289ff.
 - ibuprofen 289ff.
 - idiosyncratic adverse drug reaction (IADR) 186, 241, 351
 - competing detoxification pathway 341
 - dose size 342
 - duration of treatment 345
 - multifactorial nature 348
 - risk 347
 - risk assessment 327ff.
 - risk–benefit analysis 357ff.
 - ifosfamide 154f.
 - imidazotriazene 148
 - iminium methide species 113
 - immune-mediated toxicity 7ff.
 - in silico* approach
 - chemical reactivity 328
 - inactivation 60
 - cytochrome P450 enzyme 47ff.
 - pharmacokinetic principle 46
 - quasi-irreversible 47
 - inactivator 45
 - cytochrome P450 enzyme 49
 - inhibitor
 - covalent 315ff.
 - irreversible 314
 - irreversible warhead 317
 - kinetic description 44
 - mechanism-based 198
 - intoxication 6
 - isoniazid 60
 - metabolic activation 106
 - isosorbide mononitrate 290
 - isothiazole ring bioactivation 249f.
- j**
- januvia 290
- k**
- ketoconazole 349
 - kinase inhibitor
 - irreversible 319
 - reversible 318
 - kinetic principle
 - inactivation 44
- l**
- L-739,010 108
 - L-745,870 112
 - L-754,394 108
 - lactam
 - bicyclic 320
 - monocyclic 320
 - β -lactam 95ff.
 - antibiotic 131, 281f., 321
 - intrinsic electrophilicity 131
 - toxicity 131
 - β -lactamase 321
 - β -lactone 320ff.
 - lamotrigine 282
 - metabolic activation 284
 - lansoprazole 291
 - lapatinib 318
 - levofloxacin 297ff., 336
 - levothyroxine 273ff.
 - leupeptin 322ff.
 - 5-lipoxygenase inhibitor 108
 - lisdexamfetamine 290
 - lisinopril 273, 294ff.
 - liver transaminase level (ALT) 364
 - losartan
 - oxidative bioactivation 298
 - lorazepam 297ff.
 - lovastatin 302f.
 - lumiracoxib 101
 - metabolic activation 102
 - lyrica 290

m

MAO-A inhibitor 61f.
 MAO-B inhibitor 61f.
 maraviroc 365f.
 MDMA, *see*
 methylenedioxyamphetamine
 medicinal chemistry
 – reactive metabolite formation 241
 MeIQx, *see* 2-amino-3,8-dimethylimidazo[4,5-f]
 quinoxaline
 meloxicam 302ff., 338
 memantine 290
 menthofuran 207
 metabolic activation 275
 metabolite identification study 234
 metabolite-intermediate (MI) complex 48
 metal chelator 93
 metal complexing functional group 96
 metformin 274
 methoxsalen 55
 methoxy 4-O-aryl quinoline
 derivative 141
 methyl sulfone 134
 N-methyl-1,2,3,6-tetrahydropyridine
 (MPTP) 64
 5-[3-methyl-1-triazenyl]imidazole-4-
 carboxamide (MTIC) 149
 methylenedioxyamphetamine
 (MDMA) 51
 methylenedioxyphenyl compound 51
 methylenedioxyphenyl motif 115f.
 – metabolic activation 117
 3-methylindole 216f.
 – bioactivation 217
 – metabolic activation 113
 2-methylindole derivative
 – metabolic activation 114
 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol
 (NNAL) 17
 4-(methylnitrosamino)-1-(3-pyridyl)-1-
 butanone (NNK) 17
 methylphenidate 290
 methylprednisolone 300
 6-(2-methylpyridinyloxy)-5-cyanopyrimidine
 derivative 139f.
 4-methylsulfonyl-2-pyridone 137
 metoprolol 273ff.
 metyrapone 97
 MI, *see* metabolite-intermediate complex
 Michael acceptor 317f.
 – reactivity 329
 mibefradil 58, 197f.
 mifepristone 56, 120
 milacemide 64

mitochondrial toxicity 349
 mitomycin 168ff.
 mitomycin C 168
 – reductive activation 171
 mitosene 168
 mitozolomide 149
 MK-0524 112
 mometasone 302f.
 monoamine oxidase (MAO) 61
 – inactivation 63
 – inactivator 62
 montelukast 273ff.
 MPTP, *see* N-methyl-1,2,3,6-tetrahydropyridine
 MTIC, *see* 5-[3-methyl-1-triazenyl]imidazole-4-
 carboxamide
 mutagenesis 1
 mutagenicity
 – drug discovery 29
 mylotarg 165

n

namenda 290
 NAPQI, *see* N-acetyl-*para*-benzoquinone imine
 naproxen 291
 NAT, *see* N-acetyltransferase
 natural product 203ff.
 nefazodone 52, 336ff., 349
 neocarcinostatin chromophore 161
 neratinib 319
 neurontin 290
 niacin 282ff.
 niacinamide 288
 nicotine 204
 nilvadipine 327
 nitrile
 – heteroaromatic 324
 nitroarene 103f.
 nitroaromatic chloromustard
 – bioactivation 175
 nitroaromatic compound
 – bioreductive activation 174
 nitrogen mustard 96, 152
 – DNA alkylation 96
 nitroquinoline mustard
 – reductive activation 176
 nitrosamine 18, 219
 – adduct with nucleic acid base 219
 – carcinogenicity 17
 nitroso-imidacloprid 60
 N^o-nitrosonornicotine (NNN) 17
 nitrosoourea 147f.
 nomifensine 189
 nonergot dopamine receptor
 agonist 340

- nonsteroidal anti-inflammatory drug
(NSAID) 186ff., 359
nortriptyline 287, 344
- o**
- odanacatib 324 eins ist wahrscheinlich ein
Tippfehler
odanacitib 326
off target 186
olanzapine 304ff., 342f.
olmesartan 339
omeprazole 277, 291
– acid-catalyzed bioactivation 146
on target 186
onglyza 324
orlistat 322f.
oseltamivir 300ff.
oxazaphosphorine 152
oxidative metabolism 145
oxidative stress
– reactive metabolite cytotoxicity 5
- p**
- p53 3
pantoprazole 291
paroxetine 51, 116, 292f.
PCI-3765 320
pelitinib 319
penem 320
penicillin G 321
pennyroyal oil 207
peptidyl aldehyde 322
PF-0299804 319
pharmacokinetic principle
– inactivation 46
pharmacokinetic/pharmacodynamic (PK/PD)
prediction 346ff.
pharmacological action 145
– reactive metabolite 145
pharmacological target 346
phenanthrene 2
phencyclidine 53
1,2,4-phenylenetriamine-based inhibitor 255
phenylhydrazine
– metabolic activation 106
PhIP, *see* 2-amino-1-methyl-6-phenylimidazo
[4,5-*b*]pyridine
pioglitazone 191, 343ff.
piperazine derivative
– 1,3-disubstituted 259f.
piperazine ring system 256
plant–animal warfare 204
PNU-10912 137
PNU-140690 137
- polycyclic azaheterocyclic compound 216
potassium clavulanate 282ff.
practolol 187
pramipexole 339f.
prasugrel 152
pravastatin 302f.
prednisolone 300
prednisone 303
pregabalin 290
primary pharmacology 190ff.
procainamide 187
proline-rich tyrosine kinase 2 (PYK2) 253
– inhibitor 254
protein adduct 49
protein kinase B (AKT) inhibitor 244ff.
protein target
– reactive metabolite 197
protein-reactive metabolite
– bioactivation of vinyl chloride 27
– bioactivation pathway of tamoxifen 21
proton pump inhibitor 145f., 277ff., 291
pulegone 207
purinoreceptor antagonist 277
pyridine-2-sulfonamide 138
pyrrolizidine alkaloid 210
– bioactivation 211
- q**
- qualitative electrophile trapping assay 227
quantitative electrophile trapping assay 230
quantitative whole-body autoradiography
(qWBA) 236
quetiapine 290, 302ff., 336
quinone 19, 52
– antibiotic 168
– anticancer drug 21
– carcinogenicity 19
– *ortho*-quinone 19
quinone imine 52
quinone methide 52ff.
quinone methide intermediate
– reactive 173
quinone methide metabolite 20
- r**
- rabeprazole 291
radicol A 318
radiolabeled metabolism 235
raloxifene 53, 292
– bioactivation pathway 295
ramipril 294ff.
ranitidine 302f., 339
reactive metabolite
– cytotoxicity 5

- detection 3, 225
 - drug-induced toxicity 71ff.
 - false positive 289
 - false structure–toxicity relationship 192
 - genotoxicity 13ff.
 - immune-mediated toxicity 7
 - metabolic activation 275
 - origin and historical perspective 1ff.
 - pharmacological action 145
 - protein target 197
 - risk assessment 329
 - toxicophore 98
 - validation 198
 - reactive metabolite analysis 269ff.
 - reactive metabolite detection 3, 225ff.
 - assay 227
 - reactive metabolite formation 8
 - drug discovery 241
 - genetic influence 5
 - rational chemistry approach 242ff.
 - structural alert 338
 - toxicophore 93
 - reactive metabolite trapping 29ff.
 - reactive metabolite–positive compound 340
 - competing, detoxification pathway 341
 - drug discovery 335
 - reductive scission
 - artemisinin 167
 - remoxipride 198f.
 - reversible pharmacology 10
 - riddelliine 212
 - risk assessment 327ff.
 - risk–benefit analysis 357ff.
 - IADR 357
 - rivastigmine 321ff.
 - rofecoxib 192ff.
 - rosiglitazone 191, 350
 - rosuvastatin 339
 - rupintrivir 319f.
- s**
- S9/NADPH-dependent mutagenic response 30ff.
 - safrole
 - bioactivation pathway 22
 - salbutamol 274ff.
 - Salmonella* reverse mutation assay 32
 - saxagliptin 324ff.
 - saxitoxin 204
 - secondary pharmacology 192
 - irreversible 189f.
 - Selzentry® 365
 - serine hydrolase inhibitor 321
 - sertraline 290
 - side effect monitoring 367
 - sildenafil 290
 - simvastatin 274, 302, 350
 - sitagliptin 290
 - SPD-304 112
 - structural alert 226, 269ff.
 - drug design 336
 - identification 225
 - reactive metabolite formation 338
 - structural alert–positive drug 303
 - structure toxicity trend 302
 - structure–toxicity relationship 337
 - false 192
 - retrospective analysis 185ff.
 - strychnine 204
 - sudoxicam 304f., 338
 - sulfamethoxazole 282ff.
 - sulfonamide 134
 - sulfotransferase (SULT) 16
 - sunitinib 346
 - suprofen 193
- t**
- TA, *see* tienilic acid
 - tacrine 364
 - tadalafil 116, 292ff.
 - tamoxifen 19, 53f.
 - bioactivation pathway 21
 - tamsulosin 303
 - targeted covalent drug 313
 - targeted covalent inhibitor 317
 - telaprevir 322ff.
 - temozolomide 149
 - terbinafine 121
 - tetrodotoxin 204
 - teucrin A 205f.
 - TFA, *see* trifluoroacetic acid
 - TFA (trifluoroacetic acid)–protein adduct 78f.
 - TFAC, *see* trifluoroacetyl chloride
 - thiabendazole
 - metabolism 112
 - thiazole 109ff.
 - oxidative ring scission 110
 - thienotetrahydropyridine 150
 - thioamide 111
 - metabolic activation 111
 - thiophene 53ff., 109
 - bioactivation 110
 - thiourea 111
 - metabolic activation 111
 - thrombin inhibitor 336
 - thrombopoietin (Tpo)
 - agonist 246
 - receptor 242

- tianeptine 197, 342f.
 ticlopidine 151, 372
 tienilic acid (TA) 82, 193
 – metabolism 83
 tiotropium 303, 339
 tirapazamine 157
 tissue binding 236
 tolbutamide 195
 tolcapone 338f., 349
 tolmetin 115
 toxicity 186
 – biomarker 369
 – clinical drug toxicity 359
 – drug-induced 71ff.
 – immune-mediated 7
 – innate electrophilicity 135
 – β -lactam antibiotic 131ff.
 – multifactorial mechanisms 196
 – rules and laws 363
 – validation of reactive metabolites 198
 toxicity risk 313
 toxicophore 93ff.
 – bioactivation 98
 – intrinsically reactive 93
 tramadol 290
 trazodone 282ff.
 – metabolic activation 286
 triazene derivative 148
 triaziquone 170
 trifluoroacetic acid (TFA) 7
 trifluoroacetyl chloride (TFAC) 7
 trimelamol 153
 trimethoprim 282ff.
 troglitazone 191, 342ff.
 trovafloxacin 297ff., 336
 tubocurarine 204
 tyrosine kinase FMS inhibitor 255f.
 tyrosine kinase inhibitor 346
- u**
 uridine diphospho glucuronosyltransferase (UGT) 338
 uridine glucuronosyl transferase (UGT) 72
- v**
 valdecoxib 194f.
 valsartan 290
 vascular endothelial growth factor receptor 2 (VEGFR2) 319
 verapamil 303
 vildagliptin 324ff.
 vinyl halide
 – bioactivation into DNA- and protein-reactive metabolites 27
 – carcinogenicity 26
 vyvanse 290
- w**
 warfare
 – plant–animal warfare 204
 warhead 315ff.
 – optimization of chemical reactivity 326
 – selection 316
 warning 367
 whole-body autoradiography (WBA) 236
 – quantitative (qWBA) 236
- x**
 xenobiotic 116
 – furan-based 107
 ximelagatran 336
- z**
 zafirlukast 112
 zolpidem 302ff., 336
 zomepirac 115

