

INDEX

- Abbreviated new drug application (ANDA), 207
Absorption, 270
Acetophenone, 343
Acetovanillone, 347
Acetylenic dimethylborane, 150
Acid–base neutralization, 257
Acid-catalyzed cleavage, 65
 reactions, 189
Active pharmaceutical ingredients (APIs), 181–182,
 222, 227, 252
N-Acylamino acids, racemization of, 126
Acylase biocatalysis, 136
Agents:
 antidiabetic, 185
 antihistaminic, 196
Alane–amine complex, 345
 α -Alkoxypropionic acid, 112
 γ -Alkoxy- α,β -unsaturated esters, 175
Alkylation, 62, 198
Alkynyl alcohols, 149
 α,β -Alkynyl ketones, 142
Allium sativum, 38
Allylglycine, 126
Alzheimer's disease, 38
Amano-PS lipase, 125
American Medical Association Council on
 Pharmacy and Chemistry (AMACPC), 356, 361
Aminoacylase bioresolution, 126
 γ -Aminobutyric acid (GABA), 68, 280
4-Amino-2-methylbutanol, 129
Amorphous solids, 208
1,6-Anhydro saccharides, 166
Analgesic alkaloid epibatidine, 60
Analytical tools, 208
Angiotensin converting enzyme (ACE), 323
Anomeric hydroxyl group, 326
Anomeric radical effect, 165
Anthracenyl ligand, 133, 155
Anticancer program, 7
Anticonvulsing agents, 280
Anti-HIV drug, 312
Anti-Markovnikov product, 162
Antiparasitic agent, 54
Anxiolytic activity, 285
Aspirin, 37
Assay media, 276
Asthma, 323
Asymmetric alkylation, 154
Asymmetric allylic substitution, 133
Asymmetric hydroformylation, 132
Asymmetric hydrogenation method, 126, 127, 129, 136
Asymmetric reduction, 142, 145
Asymmetric synthesis, 312, 313
Atopic (hereditary) dermatitis, 339
Automated laboratory reactors, 261
Automotive industry, 219
Ayurvedic medicine, 311
Azacarbonyl, 337
Azeotropic water vapors, 198
2,2'-Azobisisobutyronitrile (AIBN), 320

- Batch production records (BPRs), 196
Bench synthetic procedure, 251
Benzaldehyde, 148
 α -Benzyloxy analog, 109
Benzo-1,4-dioxanes, 73
Bicyclic isoxazolidine saccharides, 174
Binaphthol-modified aluminum hydride reagent, 147
Bioactive carbohydrates, 2, 162, 169
Bioactive molecules, 6, 7
Biocatalysis, 122, 124–126
Biochemistry, 282
Biodiversity, 273
Bioefficacy enhancers, 38
Biogenetic pathway engineering, 42
Biological active oligosaccharides, 161
Biological assays, 204
Biological mechanisms, 51
Biological oxidations, 301
Biomolecules, 7
Biopharmaceuticals, classification system, 214
Bioresolution, of an ester, 123
Biosensor, 43
Bis(2-chloromethyl) carbonate (BTC), 345
Bisurea derivative, 345
Bristol-Myers Squibb, 113, 214
British Hydrodynamics Research Group, 258
Broad-spectrum antibiotic, 62
 α -Bromoacetals, 172
Bromo derivative, 341
Bromoetherification, 172
2-Bromo-3-methylthiophene, 288
t-Butyldimethylsilyl chloride, 83, 184
tert-Butyldimethylsilyl ether, 326
- Calibrated dipsticks, 252
C-alkyl glycoside, 163, 164
Carbamoyl chlorides, 345
Carbohydrate:
 isosteres, 173
 processing enzymes, 162
Carbon–carbon bond-forming reactions, 67
Carbon-linked disaccharides, 169, 170
Carbon-linked oligosaccharides, 168
Cardiovascular disorders, 315
C-aryl glycosides, 166
C-aryl heptose sugar, 167
Catalysis:
 mechanism of, 130, 247
 technology, 122
Catalyst deactivation, 130
Catalytic hydrogenation, 322
Catalytic technology, 121, 124
Catch-and-release technique(s), 52, 85
Cefpodoxime proxetil, 194
Cell-based assay, 112
Cell surface oligosaccharides, 161
Central nervous system (CNS), 311
C-glycoside sulfones, 161, 165
Chain terminating nucleotide analog, 193
Chemical process development, 251, 252
Chemical research, 310
Chemical space, 272
Chemie Grunenthal, 362
Chemistry manufacturing and control (CMC), 368
Chemocatalysis, 124
Chemotherapeutic agents, 279
Chiral catalysis method, 123
Chiral catalysts, 122
Chiral catalytic technologies, 121, 124
Chiral isomer, 121
Chiral propargyl alcohol (CPA), 142, 148, 154, 157
 synthesis, 155
Chiral tetrahydrofurans, 325
Chiraphite, 133
Chiron, 174
Chloramphenicol-3-palmitate, 202
Chlorofluorocarbons (CFCs), 234
Chronic asthma, 325
Ciglitazone, 93
Cipla, 312
Circular dichroism (CD), 42
Clean Air Act (CAA), 234
Clinical development program, 369, 370, 374
Clinical research, 360
 ethics, 357
Clinical seizures, 279
Code of medical ethics, 356
Column chromatography, 190, 328, 345
Column chromatographic purifications, 87, 184, 189
Combination:
 drugs, 36
 therapies, 39
Combinatorial chemistry, 273, 275
Compound:
 libraries, 267
 purity, 275
 solubility, 276
 stability, 276
Computational chemistry, 269
Computer-aided drug design (CADD), 204
Concomitant therapy, 371
Condensation reaction, 192
Contract manufacturing organizations (CMOs), 226
Contract research organizations (CROs), 232
Council of Scientific and Industrial Research (CSIR), 311
CrossFire Beilstein database, 271
Cryogenic reactions, 327
Crystalline carbochromen hydrochloride, 213
Crystallization, 210, 252, 328
Current good manufacturing practice (cGMP), 222, 310
CMC (current medicinal compounds) database, 271
Cytochrome P450 systems, 301

- Darvon alcohol–LAH complex, 145
 Data analysis, 255
 Dean–Stark apparatus, 72
 Decarboxylation, 62
 Denitrification, 241
 Department of Health and Human Services (DHHS), 360
 Design of experiment (DoE), 254
 Desmethyl derivative, 305
 Desmethyltiagabine, 288
 Diabetes mellitus, 91
 Diastereomeric mixture, 338
 Diastereomers, 152, 339
 Dibromoalkene, elimination of, 337
 Diethylcarbamoyl chloride (DECC), 316
N,N-Diethylurea, 317
 Differential scanning calorimetry (DSC), 203
 Dihydroxytiagabine, 298
 Dimerization, 56
 Dimethoxymethane, 148
N,N-Dimethylamine hydrochloride, 347
 Dimethyl sulfoxide (DMSO) solution, 204, 276
 Dimethylethyl amine (DMEA), 345
o-Diphenylphosphinobenzoic acid, 133
 Dioxapyrrolomycin, 62
 1,3-Dioxolane Grignard reagent, 61
 Discovery route, 325, 326
 Distillation, 52
 DMDO oxidation, 80
 DNA shuffling, 42
 DNBP process, 242
 Dose–response assessment, 239
 Dow Chemical Company, 243
 Dr. Reddy's Laboratories, 214
 Drug:
 development cycle, 226
 discovery, 265, 266, 268
 discovery process, 267
 discovery program, 202
 herbal, 3, 6, 43
 metabolites, 301
 rifamycin, 39
 safety, 366
 Drug-metabolizing enzymes, 37
 Dynamic kinetic asymmetric transformation (DYKAT), 134

 Electrolytic conductivity, 201
 Electron spray ionization mass spectrometry (ESI-MS), 42
 Electronically activated metalloporphyrins, 303
 β -Elimination strategy, 157, 158
 Elixir sulfanilamide, 361
 Enantiospecific biocatalyst, 123
 Enantiospecificity, 123, 125
 Enol ester, 172
 Enone reduction, 173

 Enzymatic hydrolysis, 173
 Enzyme inhibition assays, 42
 Epilepsy, 279, 285
 Epileptic seizures, 279
 Epimaritidine, 59
 Epimeric mixture, 333
Epipedobates tricolour, 60
 Erlenmeyer condensation chemistry, 136
 Ester hydrolysis, 260
 Ethnopharmacology, 7, 36
 Ethyl 3-amino-3-phenylpropionate, 124, 125
 Ethyl chloroacetate, 257
 Ethyl 2-ethoxy-4-methylbenzoate, 185
 Etodolac ester, 189
 Euglycemic activity, 103
 Excretion, 270

 Federal Food, Drug and Cosmetic Act (FFDCA), 362
 Fermentation broth, 122
 Ferrier reaction, 166
N,O-Ferrocene ligand, 155
 Five-membered ring hemiketal, 162
 Flash chromatography, 146
 Food and Drug Administration (FDA), 39, 221, 360, 368
 Food and Drug Administration Modernization Act, 372
 Forced-flow planar chromatography (FFPC), 40
 Freeze-crystallization techniques, 190
 Friedel–Crafts acetylation, 316
 Fries migration, 317
 Fries rearrangement, 349
 Fully integrated pharmaceutical companies (FIPCO), 221
 Furan, 168

 Gamma-aminobutyric acid (GABA), 280
 transaminase, 280
 GABA–benzodiazepine receptor, 280
 Gas chromatography, 258
 GATT agreement, 350
 General Considerations for Clinical Trials, 374
 Genetic manipulation, 42
 Genotoxicity, 367
Ginkgo biloba, 38
 GlaxoSmithKline (GSK), 112, 214
 Glitazones, 94, 107
 D-Glucose, 313
 Glucose-lowering activity, 95
 Glycals, 166
 Glycidyl ether, 338
 Glycosidic saponins, 7
 Glycosyl amino acids, 175, 176
 Good manufacturing practice (GMP), 364
 system, 365
 Good clinical practice (GCP), 369
 Good laboratory practice (GLP), 310, 365

- Green chemistry, 247
Grignard reaction, 327
Grignard reagent, 288, 289, 328, 331
Grinding, 195
- Handcrafted compounds, 274
Hazard operability (HAZOP) analysis, 196
Hazardous air pollutants (HAPs), 234
Heck reactions, 68
Hemiketal, 163
Henry reaction, 60
Heterogeneous nucleation, 211
HexaPhemp, 130
High performance liquid chromatography (HPLC) analysis, 40, 304, 323, 344
High temperature liquid chromatography (HTLC), 41
High-vacuum distillations, 184
HKR protocol, 318
Homeopathy, 3
Homologative precursor, 169
Homopropargyl alcohol, 331
Homopropargylic system, 169
Horner–Wadsworth–Emmons coupling, 83
Hydroboration–oxidation reaction, 321
Hydrochlorofluorocarbons (HCFCs), 234
Hydrogenation, of aldehydes, 129
Hydrogen bonding, 210
Hydrolytic kinetic resolution, 315, 327
cis-Hydroxylation, 168, 169
2-Hydroxy-4-methylbenzoic acid, 185
Hydroxy metabolite, 305
cis-4-Hydroxynipecotic acid, 281
4-Hydroxy pipercolates, 126
5-Hydroxy tiagabine, 296
Hydroxy ureidyl moiety, 328
Hygroscopicity, 202
Hygroscopic substances, 204
Hyphenated techniques, 42
Hypoglycemic agents, 185
Hypotriglyceridemic activity, 115
- Identification:
 of different polymorph, 202
 of metabolites, 302
Idiosyncratic reactions, 280
Immobilization, 52
Immobilized reagents, 52, 55
Immobilized triphenylphosphine, 61
Immunomodulator additives, 4
In vivo assays, 280
Indian Institute of Chemical Technology, 311
Indian pharmaceutical sector, 310
Industrial nitration processes, 243
In-process analytical tools, 252
In-silico screening, 268
Insoluble oxidants, 54
Insulin sensitizers, 92–94, 116
Insulin-dependent diabetes mellitus (IDDM), 91
Intellectual property, 124, 125, 137
International Code of Medical Ethics (1949), 358
International Conference on Harmonization (ICH), 363
Intramolecular nitrene cyclo-addition (INC), 174
Intramolecular oxime olefin cyclo-addition (IOOC), 174
IR microscopy, 209
IR spectroscopy, 209
Isodrimeninol, 53
Isotretinoin, 190, 192
Isoxazolidine-fused saccharide, 174
- Jacketed vessel, 228
Jacobsen's kinetic resolution, 331
Japanese drug, 44
Jellylike glossy mass, 346
- Ketotiagabine, 299
Kolbe electrolysis, 128
- β -Lactam antibiotics, 189
Leaching, 211
Lead optimization, 202, 311
Leukotriene B-4, 157, 323
Lewis acid, 338
Library metrics, 267, 268, 277
Ligands:
 chiral, 149, 150
 chiral amino alcohol-based, 154
 chiral bisphospholane, 127
 chiral disulfide oxazolidine, 154
 kelliphite, 133
 peroxisome proliferator-activated receptor (PPAR), 92
Lindlar's reagent, 169
Lipase:
 biocatalysis, 125
 bioresolution, 124
Lipophilic derivatives, 281
Liquid chromatography/mass spectrometry (LC–MS), 288
Lithium diisopropylamide (LDA), 186
Logical serial development, 374
Low-temperature NMR spectroscopy, 323
Lyophilization technique, 190
- Magnetic stirring bar, 145, 148
Mannich reaction, 343, 347
D-Mannitol, 212, 329
Mannose diacetonide, 164
Maximum achievable control technology (MACT), 234
Max-Planck Institute for Molecular Biology, 2
Medical ethics, 356, 358, 359
Medical research, regulation of, 360

- Medicinal chemistry:
 programs, 272
 research, 273
- Medicinal plants:
 bioengineering of, 42
 molecular farming, 42
- Medicinal systems, 1
- Metalloporphyrins, 301
- p*-Methoxybenzyl alcohol, 134
- Methyl *tert*-butyl ether (MTBE), 254
- Methyl-6,7-dimethoxy-4-ethyl- β -carboline-3-carboxylate (DMCM), 282
- 3-Methylsuccinamic acid, 129
- Metric-designed library, 277
- Mettler Toledo-PVM (particle vision and measurement), 251
- Mettler Toledo RC1 (reactor calorimeter), 254
- Michael–Wittig reaction, 173
- Microbial transformations, 155
- Microencapsulation methods, 52
- Micromixing time, 260
- Microwave techniques, 63
- Miniaturization technologies, 52
- Mitsunobu coupling, 325
- Mitsunobu reaction, 329
- Modulating membrane ion channels, 280
- Moiety:
 Het, 104
 hydrophobic, 107
 lipophilic, 281
 sugar, 168
- Molecular diversity, 272
- Multiple-dose study, 371
- Multireagent processes, 52
- Multistep organic synthesis, 51
- National Chemical Laboratory, 311
- National Institutes of Health (NIH), 7
- National Pollutant Discharge Elimination System (NPDES), 239
- New chemical entities (NCEs), 202, 221
- New drug application (NDA), 364
- Nipecotic acid moiety, 300
- NMR spectrum, 148, 298
- NOE experiments, 321
- Non-insulin-dependent diabetes mellitus (NIDDM), 91
- Nonstoichiometric hydrates, 207
- Norarmepavine, 59
- Novel therapeutic agents, 309
- Nuclear magnetic resonance (NMR), 42, 289
- Nucleophilic substitution reaction, 338, 342
- Nucleoside reverse transcriptase inhibitors, 39
- Nuremberg code, 357, 358
- Offshoring, 219
- Olefinic alcohols, 164
- Oligomerization, 56
- One-pot processes, 52
- Open-chain dihydrocinnamic acid analog, 110
- Operational times, 252
- Optimization:
 analysis, 255
 protocols, 204
- Optimum pressure laminar chromatography (OPLC), 40
- Oral hypoglycemic agents (OHA), 91
- Organic semiconductors, 216
- Organic volatile impurity (OVI), 252
- Organisation for Economic Co-operation and Development (OECD), 366
- Orphan drug regulations, 373
- Oxazaborolidine(s), 146, 150
- Oxazaborolidine-catalyzed enantioselective reduction, 146
- Oxidative cyclization, 164
- Oxidative degradation, 298
- Oxometalloporphyrins, 302
- Oxybenzylglycines, 113
- Ozone depleting compounds (ODCs), 41
- Palladium-based catalysts, 133
- Parkinson's disease, 280
- Patent:
 implications, 213
 polymorphs, 182
 position, 271
 protection, 214
- Paxil (paroxetine hydrochloride), 214
- PPAR γ (peroxisome proliferator-activated receptor) ligands, 92, 94
- Person-specific drugs, 3
- Pfizer, 107
- PhanePhos–ruthenium diamine, 130
- Pharmaceutical industry, 220, 222, 310
- Pharmaceutical process development, 252
- Pharmacokinetic parameters, 111, 366, 370
- Pharmacology, 282, 368
- Phase transfer catalysts, 297
- Phenoxycarbonate protecting group, 333
- Phenyl ligand, 133
- Phenyl ring, 107
- Phenylalanine analogs, 126
- Photoisomerization, 191
- Photosensitizers, 191
- Phthalimidovinylglycinol, 134
- Pioglitazone, 113
- Piperine, 39
- Plasmodial pigment, 54
- Polishing, 195
- Pollution control devices, 237
- Pollution prevention, 238
- Polyethylene glycol support (PEG), 65
- Polyhydroxyfuran derivatives, 335

- Polymer-bound species, 52
Polymer catch-and-release technique, 59
Polymer-supported amine base, 60
Polymer-supported borohydride reduction, 60
Polymer-supported borohydride, 58
Polymer-supported chlorite, 85
Polymer-supported cyanoborohydride, 59, 61
Polymer-supported ester, 80
Polymer-supported permanganate, 62
Polymer-supported phosphazene base, 55
Polymer-supported reagents, 57, 63
Polymer-supported reductant, 57
Polymer-supported sulfonic acid, 61
Polymer-supported sulfonyl transfer reagent, 67
Polymer-supported triphenylphosphine, 85
Polymorphism, 182, 201, 212, 215, 216
Polymorphs, 213, 216
Porphyrin-assisted oxidation, 296
Porphyrin-mediated oxidation, 305
Potential polymorphic systems, 209
Preclinical development, 364
Preclinical evaluation, 367
Preclinical research phase, 266, 269
Principal component analysis (PCA), 53
Process:
 analytical technology, 252
 development cycle, 183
 optimization program, 192
 research and optimization, 311
 robustness, 251
Process chemistry, 233
Prochiral ketones, 129
Prochiral olefins, 127
Propargyl alcohol derivative, 339
Propargyl alkoxide, 330
Propargylic ketones, 156
Protection–deprotection sequences, 326, 327
Protic organic solvent, 189
Pseudodilution, 55
Pseudopolymorphs, 206
Pseudosugar, 173
Psoriasis, 339
Pungent solution phase, 56
Pure Food and Drug Act, 361
Pyranoside-based spiroacetal, 170
Pyridoxal-dependent transamination, 280

Quantum chemical calculation, 42
Quaternary chiral center, 319
Quaternary salt, 343, 348
Quinidine, 362
Quinone, 243
Qualitative identification, different polymorphs, 202

Radical cyclization, 172
Radical ring-opening reaction, 319
Ragaglitazar treatment, 111

Ranbaxy, 214
RCM reaction, 321, 322
Real-time analysis, 247
Receptor transactivation assay, 104
Red papulovesicular oozing lesions, 339
Reduction:
 acetylenic ketones, 146, 148
 alkynyl ketones, 147
 cyano group, 345
Reductive cleavage, 155
Reductive ozonolysis, 330
Regiospecific process, 194
Regulatory concerns, 213
Repeatability, 195
Reproducibility, 195
Resin-bound phosphonium salt, 85
Resveratrol, 37
Retrosynthetic analysis, 288, 334
Rhodium–Chiraphite system, 132
Rhodium–DuPhos catalysts, 127, 136
Rhodium–ethyl-DuPhos, 137
Rhodium–phosphite catalysts, 132
Ring-closing metatheses (RCM), 319, 313
Rosiglitzone, 103
Runaway reaction, 196
Ruthenium–bisphosphine–diamine catalysts, 129
Ruthenium–chiral bisphosphine complexes, 129

Safety pharmacology studies, 367
Scaffold precursors, 323
Seeding, 210
Selenium-based resin, 77
Selenium-mediated ring, 57
Self-optimization processes, 52
Serendipity, 276
Silica-gel column chromatography, 158
Silylating agent, 184
Silyl-protecting groups, 327
Simmons–Smith reaction, 320
Simulated moving-bed chromatography (SMBC), 40, 41
Single-dose toxicity studies, 366
Singleton, 273
Skin disorders, 339
Slow-reacting substance of anaphylaxis (SRS-A), 324
SmithKline Beecham, 110
Sodium hydroxide, 258
Solid-liquid separator, 228
Solid-phase extraction (SPE), 40
Solid-supported reagents, 52, 58
Solubility, 270
 measurements, 254
Solution-phase glycosylation, 78
Solution-phase reagents, 63
Solution-phase techniques, 78
Solvent recovery system, 238

- Specialized pilot-plant equipment, 257
Spiroacetal saccharides, 172
Spiroproline derivatives, 323
Splash monitoring, 210
Staggered extension process, 42
Stemoamide, 313
Stereochemical features, 327
Stereoisomeric tetrahydrofuran derivatives, 335
Stereoselective dihydroxylation, 173
Stereoselective reduction, 59, 168, 169
Stetter reaction, 340, 341, 346–348
Stevens–Johnson syndrome, 280
Stille reactions, 68
Stoichiometric hydrates, 207
Stoichiometric reagent, 122
Stoichiometric reducing agents, 122, 129
Stoichiometric technology, 124
Sugar-derived chirons, 174
Sugar-linked iodolactones, 174
Sulfone derivative, 339
Supercritical fluid extraction (SCFE), 41
Surrogate endpoint, 370
Swern oxidation conditions, 321
Synergism, 36
Synergistic material, 4
Synthesis:
 alkynyl Furan, 336, 337
 chiral propargylic alcohol, 151
 metabolites, 285
 regioisomers, 291
 symmetrical analogs, 285
 unsymmetrical analogs, 288
 vinyl ketone, 343
Synthetic drugs, 7
Synthetic metalloporphyrins, 302
Synthetic Methodology Assessment for Reduction
 Techniques (SMART), 248
Synthetic organic chemistry, 312
Syphilis, 357

Tandem mass spectrometry (TMS), 42
Tartaric acid, 157
Tetrabutylammonium fluoride (TBAF), 85, 153
Tetrahydrofuran (THF), 331
Tetrahydropyran (THP), 331
Therapeutic agents, 92
Therapeutic exploratory, 374
Thermococcus litoralis, 127
Thermogravimetric analysis (TGA), 208
Thiophene, 164

 β -Thymidine, 312
Tiagabine, 285, 292, 297
 spectrum, 298
Toxicokinetics, 366
Toxicology, 270, 368
 program, 366
Traditional medicine, 3
Traditional wisdom, 3
Transition metal catalysts, 191
Trap–react–release protocol, 77
3,4,5-Trimethoxyacetophenone, 343
Triphosgene, 345
Turnkey process for celioprolol, 316
Tuskegee Syphilis Study, 357
Two-step oxidation protocol, 53

 α,β -Unsaturated ester, 330
U.S. drug regulatory process, 364
U.S. Environmental Protection Agency (EPA), 234
U.S. federal regulations, 360
U.S. Food and Drug Administration
 (FDA), 203, 310
United Kingdom Prospective Diabetes Study
 (UKPDS), 91
Urea derivative, 316, 337, 345

Vinyl chloride, 158
Vinyl ketone, 348
Virtual chemistry, 271
Volatile organic compound (VOC), 41
Volumetric productivity, 123

Wacker oxidation, 162
Wastewater treatment units, 238
Wittig olefination, 322, 330, 334
Wittig reaction, 85, 320
Wittig ylide, 169
World Health Organization (WHO), 91, 310
World Medical Association (WMA), 358
Wyeth Pharmaceuticals, 222

D-Xylose, 312

Zantac, 214
Zemplan deacetylation conditions, 329
Zidovudine, 312
Zinc alkynylide, 151
Zinc complexes, 296
Zinsser Sophas robotic platform, 67
Zymosan-inducing paw edema, 365

