

# Index

- A**  
Absorption, distribution, metabolism and excretion (ADME), 501  
Acheflan®, 24  
Aché Pharmaceutical Laboratories, 25  
Achmatowicz rearrangement (AR), 270  
    bicyclic dipyranyl synthon, 279  
    carbocyclic ring closure, 278  
    chiral oxopyranyl scaffolds, 276  
    D-glucoside, 271  
    englerin A, 277  
    furylcarbinols, 271  
    geniposide, 275  
    heterocyclic intermediates, 279  
    2-hydroxy-*exo*-brevicomine, 274  
    m-CPBA, 277  
    musellarin A, 278  
    olephinic dipolarophile, 275  
    oxidative enzymes, 273  
    oxonium derivative, 275  
    papulacandin D, 272  
    pyran rings, 278  
    sharpless epoxidation reagents, 273, 280  
Activator protein 1 (AP-1), 167, 172  
Active molecule encapsulation techniques, 410  
Active pharmaceutical ingredients (API), 265  
Active principles, 113, 135  
Acyclic 1,3-dicarbonyl compounds, 254  
Adequate Double Quantum Transfer Experiment (ADEQUATE), 489, 490  
Adverse drug reactions (ADR), 501  
*Agastache rugosa*, 40  
Aged black garlic (ABG), 118  
Aged garlic extracts (AGE), 119  
Aglycones, 165  
*Agrobacterium rhizogenes*, 57  
*Agrobacterium tumefaciens*, 60  
Alky resorcinol glycosides, 226  
Allene  
    keto ester, 255  
     $\delta$ -position, 254  
*Allium sativum*, 15  
    compounds, 15 (*see* Garlic)  
    principle, 15  
Alpinetin (Alp), 181, 182  
Alzheimer disease, 6, 439  
Amentoflavone (Afla), 176  
American Heart Association (AHA), 122  
Ampelopsin (Amp), 185  
Amphotericin B, 39  
Anthocyanidins, 163  
    C1, 188  
    C3G, 187  
    Mal, 188  
    Mal3OG, 188  
    Pel, 188  
    Peo, 188  
Anthracyclines, 319  
    doxorubicin, 318  
    liposomes, 318  
    sabarubicin, 320  
Antibody-drug conjugates (ADCs), 314  
Anticancer agents  
    marine derived non-nucleoside agents, 322, 323  
    microbial-derived, 316, 318, 319  
    nucleoside-derived agents, 320–322  
    polycyclic xanthone, 251, 252  
Anti-*Candida* therapy, 40  
Antifungal activity, 36, 41, 42  
    human fungal pathogens, 35

- Antifungal activity (*cont*)  
 plant extracts, 35  
 secondary metabolites, 37
- Antifungal agents, 40
- Antifungal susceptibility methods  
*Candida* species, 39  
 diffusion method, 38  
 dilution methods, 38  
 MIC and MBC, 39
- Antihyperlipidemic activity, 102, 103
- Antimicrobials  
*H. perforatum*, 60  
 metabolites, 61  
 root cultures, 60  
 secondary metabolites, 60
- Antioxidant compounds, 96, 97
- Antitumor agents  
 camptothecin derivatives, 312–314  
 derivatives, 314  
 homoharringtonine, 315  
 taxol derivatives, 315  
 vinca alkaloid derivatives, 310–312
- Antitumor drug  
 eribulin, 287  
 halichondrins, 286  
 HB, 286
- Apigenin (Api), 177
- Arachidonic acid (AA), 4, 168
- Arbutin, 485, 486
- Aristolochia* genus, 4
- Artichoke, 21
- Artificial intelligence, 348
- Aspergillus* spp. infections, 45
- Astragalol (Ast), 181
- Autoscaling, 89
- Ayurvedic medicine, 35
- Azole antifungal agents, 39
- B**
- Basil hairy root cultures, 62
- Benign prostatic hyperplasia (BPH), 12
- Bioactive compounds, 393
- Bioavailability, 423, 436, 437, 440, 445
- Biochemical pathway of signal transduction, 170
- Biodiversity, 2, 309
- Biofilms, 39
- Biological activity, 10  
 musellarins, 278  
 paeoveitols, 241, 242
- Biomass, 269
- Biosynthetic pathways, 37, 309
- Biotechnological system, 57
- Bisdemethoxycurcumin (BDMCur), 114
- Black pepper, 134–136
- Blood-brain barrier (BBB), 177
- Boehringer Ingelheim (BI), 214
- Bone marrow-derived macrophages (BMDM), 188
- Box-Behnken design, 78
- Brassard-type dienes  
 aldehydes, 240  
 dihydrokavain, 241  
 kavain, 240, 241  
 synthetic application, 240
- Brassica oleracea* (Brassicaceae), 132
- Broccoli, 132–134
- Bryostatins  
 allylstannate, 290  
 boron-aldol condensation, 293  
*Bugula neritina*, 289  
 C ring subunit, 294  
 functionalized C-ring fragment, 292  
 functionalized ring A, 290, 291  
 homoallylic alcohol, 291  
 hydrolysis, 292  
 medical applications, 289  
 Mukaiyama aldol reaction, 291  
 olefin, 291, 292  
 ozonolysis, 295  
 PKC, 289  
 PKS-I, 289  
 PPTS, 295  
 pyran, 290  
 ring A subunit, 292, 294  
 scalable total synthesis, 295  
 structure, 290  
 synthesis, 293
- Butyrylcholinesterase (BChE) inhibitory activity, 99, 100
- C**
- Caffeine, 20
- Callus cultures, 57
- Calyxin I analogue, 257
- Camptothecin derivatives, 312–314
- Cancer drug delivery, 444
- Carbon-carbon double bonds, 246
- Carbonyl allylboration, 245
- Catechins, 163
- Catechol-O-methyltransferase (COMT), 165
- Cell adhesion molecules (CAMs), 170
- Centralised procedure, 368
- C-glycosyl compounds  
 aglycon assembly, 267  
 1,2-anhydroxyranoses, 263

- Ar group, 266
- arylaluminum reagents, 267
- aryl and heteroaryl aglycons, 259
- C-aryl glycols, 262
- C-C bond formation, 259
- $\alpha$ -C-glycosides, 262
- $\beta$ -C-glycosides, 261
- C-nucleophilic reagents, 259
- Ferrier rearrangement, 261
- gluconic acid lactone, 261
- Heck-type reaction, 259, 260
- pharmacy and medicine, 263
- 2,3-unsaturated pyranoses, 260
- Chalcone glycosides, 191
- Chalcones, 480, 481
  - 5B, 191, 192
  - FlkA, 192
  - Ibc, 191
  - L2H17, 190
  - LicoC, 192
  - Phl, 191
- Chamomile, 18
- ChemGPS, 354
- Chemical similarity analysis, 339
- Chemical space analysis, 338, 339
- Cheminformatics
  - chemical similarity analysis, 339
  - chemical space analysis, 338, 339
  - chemical structure formats
    - anthranilic acid, 336
    - connection table, 335
    - mol2, 337
    - PDB, 337
    - smiles code, 335
  - definition, 334
  - molecular descriptors, 335, 337
  - molecular fingerprints, 338
- Chemokines, 169, 170
- Chemometric tools, 74
- Chinese Herbal Medicine (CHM), 355
- Chiral oxopyranyl scaffolds, 276
- Cholesterol-reducing activity, 103
- Chromatographic fingerprints, 83
  - autoscaling, 89
  - BChE, 99, 100
  - column centering, 89
  - correlation graphics, 90
  - COW, 89, 101
  - CV, 92
  - DPPH, 97
  - HCA, 90, 92
  - HPLC fingerprint data, 94
  - HPLC-DAD, 101
  - MAO-A, 97, 99, 100
  - multivariate calibration, 91
  - OPLS regression modeling, 98
  - PCA, 90, 91
  - peak alignment, 88
  - PFC, 97
  - PLS, 93
  - pretreated, 88
  - regression coefficients, 93, 97
  - RMSECV, 92
  - RMSEP, 95
  - SIS-iPLS, 96
  - supervised data analysis techniques, 91
  - training set, 92
  - unsupervised data analysis, 89
  - UPLC-DAD, 89, 90
  - warping, 89
- Chrysin (Chr), 175
- Circular dichroism (CD), 209
- Cisplatin, 183
- Citrin, 163
- <sup>13</sup>C-NMR
  - C-1 epimer, 490
  - C-19 methyl group carbon, 478
  - coupling constants, 489
  - 2,2-dimethyl-dehydro-pyran, 481
  - HC-COBI and HMBC, 469
  - isotopologues, 488
  - 3,5-*O*-dicaffeoylquinic acid, 490
  - pregnane, 477
  - $\gamma$ -steric effect, 491
  - urechitol A, 470
- Coacervation methods, 430
- Colloidal carriers, 392
- Column centering, 89
- Column chromatography
  - apolar stationary phase, 81
  - Eddy diffusion, 83
  - gradient elution, 81
  - HETP, 82
  - HPLC, 80, 82
  - intermediately polar stationary phase, 81
  - mobile phase, 81, 82
  - principle, 81
  - reversed-phase LC, 81
  - stationary phase, 82
  - UHPLC, 83
- Committee on Herbal Medicinal Products (HMPC)
  - coopted members, 373
  - EMA, 366, 373
  - guidance
    - non-clinical efficacy and safety, 382, 384
    - quality, 375, 383

- Committee on Herbal Medicinal Products (HMPC) (*cont*)  
 herbal substances, 375, 382  
 legal tasks, 372, 373  
 MLWP, 374  
 monographs, 367 (*see also* Monographs)  
 ORGAM DG, 373  
 public statements, 384  
 Q DG, 373  
 scientific committees, 372
- Common Technical Document (CTD), 369, 385
- Complementary and alternative medicines (CAM), 496
- Compound Structure Identification: FingerID (CSI:FingerID), 219
- Comprehensive Natural Products Chemistry, 209
- Computer-aided drug discovery (CADD), 333–334
- Conventional healthcare practitioners (CHP), 503–505
- Conventional solid-liquid extraction protocol, 227
- Cordia verbenacea*, 24, 25
- Correlation Optimized Warping (COW), 89
- Cross-validation (CV), 92
- Cryptococcosis, 46
- Curcuma domestica*, 113
- Curcuma longa*, 113
- Curcumin, 40  
*See also* Tumeric
- Cyanidin-3-O-glucoside (C3G), 187
- Cycloartanes, 478
- Cyclooxygenase-2 (COX-2), 115
- Cynara scolymus*, 21, 22
- Cytokines, 167, 169
- D**
- Daidzein (Dai), 189
- Dapagliflozin, 264, 265
- Dark chemical matter (DCM), 213–216
- Decentralised procedure (DCP), 368
- Demethoxycurcumin (DMCur), 114
- Density functional theory (DFT), 466
- 3-Deoxy-D-manno-2-octulosonic acid (KDO), 280  
 ammonium, 282  
*Aureobacterium barkerei*, 280  
 chemical synthesis, 281  
 chemo enzymatic synthesis, 281  
 CMP-KDO, 280  
 Danishefsky's HDA synthesis, 283, 284  
 D-arabinose, 281–283  
 2,3-4,5-di-O-isopropylidene-D-arabinose, 282  
 di-tert-butyl oxaloacetate, 281  
 HDA, 283  
 Horner-Wadsworth-Emmons reaction, 285  
 large-scale synthesis, 285  
 lithium enolate, 282  
 oligosaccharides, 280  
 synthesis, 284  
 Wittig reaction, 283
- Dereplication, 220–223
- Dermatomycoses, 38
- Dermatophytes, 38  
*Croton urucurana*, 44  
 epidermomycoses, 43  
 fungal infections, 43  
 pathogenic fungi, 43
- Diabetes mellitus (DM), 129
- Diallyl trisulfide (DATS), 120
- Diels-Alder cycloaddition, 245
- Diferuloylmethane, 114
- Diffusion method, 38
- Dihydropyrans, 248
- Dihydropyran synthons, 234
- Dilution methods, 38
- Dinimbidol ether, 467
- Diode-array detectors (DAD), 83
- Docosahexaenoic acid (DHA), 121
- Docosapentaenoic acid (DPA), 121
- Domino reaction  
 cycloaddition reactions, 242  
 definition, 242  
 4*H*-chromenes, 255  
 organocatalysts, 242
- Double emulsions (DE) complex systems, 421
- Drug discovery  
 combinatorial synthesis, 74  
 HTS, 74  
 machine learning, 348  
 VS, 357
- Drug polymeric encapsulation, 411
- Drug release pattern  
 chitosan-TPP NPs, 438  
 encapsulation studies, 441–442  
 glycol based chitosan, 439  
 intravenous injection route, 439  
 pH environment, 436  
 polyphenols, 436–438
- Dynamic Time Warping (DTW), 89
- E**
- Ebers Papyrus*, 73

- Ecopharmacognosy, 511  
Eddy diffusion, 83  
Eisai Research Institute (ERI), 286, 287  
Electrophoretic mobility assay (EMSA), 7  
Electrospray ionization, 84, 85  
Elicitor, 58  
Ellagic acid, 41  
Ellmann microplate assay, 6  
Embelin analogues, 243  
Empagliflozin, 266  
Emulsification process  
  advantages and drawbacks, 423  
  double emulsion, 421  
  emulsification-ionic gelation, 421  
  emulsion-diffusion method, 420  
  liposomes, 424  
  niosomes, 424  
  protection, 422  
  solvent evaporation, 417–420  
Emulsification-ionic gelation, 421  
Emulsion-diffusion method, 420  
Emulsion solvent diffusion method, 420  
Encapsulation, 403  
  active phytochemical, 407  
  formulations, 419  
  microencapsulation, 410  
  microspheres, 418  
  nanoprecipitation, 411, 415  
  organs and administration routes, 417  
  particle size, 416  
  polymeric nanoparticles/nano-structured,  
    412–415  
  principles, 410  
  process, 408  
  solvent evaporation, 417  
  solvent extraction, 417  
  structures, 410  
Endoplasmic reticulum stress, 212  
Endothelial cell selectin (E-selectin), 170  
*Ent-kaurenes*, 474, 475  
Enzyme-assisted aqueous extraction  
  (EAAE), 398  
Enzyme-assisted cold pressing (EACP), 398  
Enzyme-assisted extractions (EAE)  
  application, 401  
  bioactive compounds, 398  
  EACP, 398  
Enzymatic pre-treatment, 398  
Epicatechin, 128  
*Epi-flemistricin B*, 466, 467  
Epigallocatechin, 128  
Epigallocatechin-3-gallate (EGCG), 185, 186  
Epothilones, 317, 318  
Epstein-Barr virus, 56  
Eribulin  
  chiral pool derived building blocks, 288  
  ERI, 287  
  HB synthesis, 287  
  retrosynthetic analysis, 287  
  structure, 287  
  THP ring, 289  
Ertugliflozin, 267  
Erva-baleeira, 24  
Ethnopharmacological information, 226  
Ethylenediamine diacetate (EDDA), 243  
Eudragit®, 420  
*Eugenia catharinae*, 226  
Eupatilin (Eup), 178  
European Medicines Agency (EMA), 366, 372  
European Union monographs, 366, 375, 386  
Extraction, 394–403  
  chemometrics, 77  
  experimental-design approaches, 77  
  LC-MS analysis, 75  
  LLE, 77  
  MAE, 76  
  metabolites, 75  
  metabolome analysis, 77  
  PSE, 76  
  SFE, 76  
  solvent, 75  
  SPE, 76–78  
  UAE, 76  
Extraction protocols, 223  
Extra Virgin Olive Oil (EVOO), 123  
**F**  
Federal Food, Drug, and Cosmetic Act  
  (FFDCA), 113  
Ferric Reducing Antioxidant Power (FRAP),  
  93, 94  
First-generation Grubbs catalysts, 247  
Fisetin (Fis), 179, 180  
Flavan-3-ols  
  Cat, 186  
  EGCG, 185, 186  
Flavanones, 163  
  Alp, 181, 182  
  Nag, 183  
  Nar, 182, 183  
  Pin, 184  
  SG, 184  
  UgoM, 184  
Flavanonols  
  Amp, 185  
  Tax, 185  
Flavokawain A (FlkA), 192

- Flavones, 163, 482, 483  
Afla, 176  
Api, 177  
Chr, 175, 176, 179  
Eup, 178  
4'-HW, 176  
ICT, 178  
Lut, 176, 177  
OroA, 178  
Tri, 178  
Vel, 177  
Vix, 176  
Won, 176
- Flavonoids  
absorption and metabolism, 164, 165  
absorption and metabolism, 166  
anti-inflammatory agents, 174  
anti-inflammatory effect, 200  
Ast, 181  
biological activities, 164  
cardiovascular diseases, 164, 192  
chalcones, 480, 481  
chemical structures, 162, 163  
compartments, 165  
Fis, 179, 180  
flavans, 483, 484  
flavones, 482, 483  
free radical scavenger effect, 173  
glycosides, 165  
hydroxyl groups, 174  
Ica, 180, 181  
intracellular signaling pathways and mediators, 193–199  
lipid metabolism, 164  
macrophages, 173  
mechanism of action, 175  
metabolites, 166  
plant growth, 162  
polyphenolic compounds, 162  
polyphenols, 164  
protein kinase and lipid kinase signaling, 174  
Quer, 200  
quercetin-3-glucoside, 200  
ROS, NO and PG, 174  
Rut, 179  
subclasses, 162  
vitamin P, 163
- Fluidized bed coating/air suspension, 435–436  
Food and Drug Administration (FDA), 113  
Fragmentation, 85  
Freeze drying, 435  
French paradox, 164  
Fuji's phosphonate, 295
- Functional foods  
black pepper, 134–136  
broccoli, 132–134  
curcumin, 113–117  
garlic, 118–120  
ginger, 130–132  
grapes, 134  
health conditions, 113  
markets, 113  
olive oil, 123–127  
tea, 127–130  
therapeutic potential, 113, 146
- Furan derivatives  
biomass transformation, 270  
chiral 2-furyl alcohols, 273  
Friedel-Crafts alkylation, 271  
HMF, 269  
monosaccharides, 269  
oxidation reactions, 269
- Fuzzy Warping (FW), 89
- G**
- Ganoderma lucidum*, 355
- Garlic  
ABG, 119  
AGE, 119  
alliin and allicin, 118  
antiplatelet and procirculatory activities, 118  
cardiovascular system, 119  
esophageal-gastric junction adenocarcinoma, 120  
gram-negative and gram-positive bacteria, 119  
human intestinal protozoan parasites, 119  
Liliaceae family, 118  
lipid metabolism, 119  
natural organosulfur compounds, 120  
organosulfur compounds, 118  
therapeutic effects, 118  
type 2 diabetes mellitus, 120
- Gastroprotective properties, 19  
Generally recognized as safe (GRAS), 114  
Genistein (Gen), 189  
Ginger, 130–132  
Gingerols, 131  
*Ginkgo biloba*, 11  
bioactive compounds, 11  
chemical and biological aspects, 11
- Gliflozins  
antidiabetic therapeutics, 264  
dapagliflozin, 265  
6-deoxy analogs, 267

- empagliflozin, 266
- ertugliflozin, 267
- O-glycosyl precursors, 264
- tofogliflozin, 268
- Glucose-6-phosphatase (G6Pase), 129
- Glutathione peroxidase (GPx), 183
- Glycine max, 17
- Grapes, 134
- Green tea, 129
- Gut microbiota, 137
  
- H**
- Halichondrin B, 286
- Halichondrins, 285
- Healthcare workforce
  - CHP, 504, 505
  - TMP, 503, 504
- Hedycoropyrans, 279
- Height Equivalent to a Theoretical Plate (HETP), 82
- Herbal-drug interaction (HDI), 501
- Herbal formulation development, 444
- Herbal medicinal products (HMP), 367, 498
- Herbal medicines, 393, 407
  - categories of products, 387
  - centralised procedure, 368
  - DCP, 368
  - efficacy, 499, 500
  - globalization, 366
  - legal regulation, 365
  - legislations, 387
  - marketing authorization and registration, 369
  - MRP, 368
  - national procedure, 368
  - preparations, 368
  - product categories, 388
  - the public, 510
  - public funding and cost, 509
  - quality, efficacy and safety, 387
  - quality, safety and efficacy, 386
  - regulation, 505–509
  - safety, 501, 502
  - stakeholders, 497
  - TM and CAM, 496, 497
- Herbal preparations, 368
- Herbal substances, 368
- Herbasec® technology, 440
- Hetero-Diels-Alder reaction (HDA reaction)
  - Brassard-type dienes, 240, 241
  - catalyst-controlled doubly
    - diastereoselective, 238
  - chiral phosphoric acid-catalyzed, 241
  - chiral substrate control, 237
- Danishefsky's diene
  - and aldehydes, 236, 238
  - glyoxals, 238
  - $\alpha$ -ketoaldehyde, 239
  - $\alpha$ -ketoesters, 239
- dihydropyranone stereoisomers, 237
- dihydropyrans, 236
- 2*H*-pyrans, 236
- (salen)Cr(III)-BF<sub>4</sub> complex, 237
- structural heterocyclic core, 236
- substrate-controlled
  - diastereoselective, 237
- $\delta$ -lactones, 239, 240
- Heteronuclear multiple bond correlation (HMBC), 473, 488
- Heteronuclear single quantum correlation (HSQC), 487
- Hierarchical cluster analysis (HCA), 90, 92
- High-density lipoprotein (HDL), 117
- High pressure/performance liquid chromatography (HPLC), 80, 81
- High-throughput screening (HTS), 74, 210
- Hit list selection
  - chemical diversity, 352
  - drug-likeness, 353
  - filtering, 353
  - PAINS motifs, 353
  - pharmacophore, 354
  - QSAR models/similarity, 352
  - Rho kinase, 354
- <sup>1</sup>H-NMR
  - arbutin, 486
  - carbinol proton, 476
  - COSY, 470
  - cycloartanes, 478
  - 2',4-dimethoxy-6'-hydroxyonchocarpin, 481
  - 5,4'-dimethoxy-(7,6:2'',3'')-6'',6''-dimethylpyranoflavone, 483
  - dinimbidiol ether, 468
  - epi-flemistrictin B*, 466, 467
  - flavone, 483
  - glycosylated metabolites, 484, 485
  - HC-COBI and HMBC, 469
  - HSQC, 471
  - 1-hydroxy-18-nor-kaur-4,16-dien-3-one, 475
  - isoskimmwallin, 479
  - 3-*o*-acetyl ceanothoic acid, 467, 468
  - 3,4-*O*-dicaffeoylquinic acid
    - methyl ester, 491
  - 3,5-*O*-dicaffeoyl-*epi*-quinic acid methyl ester, 491

- <sup>1</sup>H-NMR (*cont*)  
 oxygen-bearing methine, 476  
 quinic acid, 491  
 skimmiiwallin, 479  
 3 $\beta$ ,14 $\beta$ ,20-trihydroxypregn-5-ene-18-oic-(18-20) lactone, 476, 477  
 3 $\beta$ ,4 $\beta$ ,5-trimethoxy-4'-hydroxy-(7,6:2'',3'')-6'',6''-dimethylpyranoflavan, 484  
 TOCSY, 485  
 urechitol A, 471  
 vinylic-proton signal, 476  
 Homoharringtonine, 315  
 HPLC fingerprint data, 94  
 Human astrocytes (hAs), 177  
 Human brain microvascular endothelial cells (hBMECs), 177  
 Human fungal diseases  
 classification, 36  
 cutaneous mycoses, 38  
 malaria/ tuberculosis, 37  
 screening process, 38  
 Human gingival fibroblasts (HGFs), 180  
 Human peripheral blood mononuclear cells (hPBMCs), 178  
 Human umbilical vein endothelial cells (HUVEC), 179  
 Hydroxytyrosol, 126  
 Hypercholesterolemia, 15  
*Hypericum perforatum*, 13, 15, 59  
 flavone derivatives, 13  
 literature reports, 15  
 principles, 15  
 Hypernated spectroscopic techniques, 210
- I**  
 Icariin (Ica), 180  
 IL-1 receptor-associated kinase (IRAK), 192  
*Ilex paraguaiensis*, 20, 21  
 Impaired fasting glucose (IFG), 129  
*In silico*  
 computational methods, 354  
 MD simulation, 356  
 molecular libraries, 339  
 telomestatin, 356  
 Inclusion criteria, 372  
 Incredible Natural Abundance Double Quantum Transfer (INADEQUATE), 489  
 Inducible nitric oxide synthase (iNOS), 115  
 Inflammation, 166, 167  
 Inflammatory mediators  
 AA, 168  
 CAMs, 170  
 chemokines, 169, 170  
 cytokines, 169  
 NO, 168  
 Intercellular adhesion molecules (ICAMs), 170  
 Interferon gamma (IFN- $\gamma$ ), 167  
 Interleukin (IL)-1 $\beta$ , 167  
 International Regulatory Conference on Herbals (IRCH), 388  
 Intracellular signaling pathways  
 AP-1 pathway, 172  
 MAPKs pathway, 173  
 NF- $\kappa$ B pathway, 171  
 STATs proteins, 171, 172  
 Invalid metabolic panaceas (IMPs), 215  
 Ionization, 84  
 Irritable bowel syndrome, 145  
 Isobavachalcone (Ibc), 191  
 Isoflavones, 17, 18, 163  
 Isoflavonoids  
 Dai, 189  
 Gen, 189  
 Gen-27, 189  
 Ono, 190  
 Pru, 190  
 Pue, 189  
 Isoskimmiiwallin, 479, 480
- J**  
 Janus kinases (JAK), 115
- K**  
 Kefir, 140, 141  
 Khat, 438  
 Kombucha, 142, 143
- L**  
 Labile natural products, 216, 217  
 Lactase phlorizin hydrolase (LPH), 165  
 Library of Pharmacologically Active Compounds (LOPAC), 212  
 Licochalcone C (LicoC), 192  
 Ligand fishing strategy, 226  
 Lipopolysaccharide (LPS), 167  
 Lipoprotein A (LPa), 120  
 Liposomes, 423  
 definition, 422  
 niosomes, 429  
 structure, 424



types, 424  
Lipoxygenase, 115  
Liquid chromatography-mass spectrometry (LC-MS), 212  
Liquid-liquid extraction (LLE), 77  
Luteolin (Lut), 176  
Lypooxygenases (LOXs), 168

## M

Machine learning, 348  
Macrolide lactone, 258  
*Malassezia* spp., 44, 45  
Malvidin (Mal), 188  
Malvidin-3-O-glucoside (*Mal3OG*), 188  
Marine derived non-nucleoside agents, 322, 323  
Marine toxin lead compound, 286  
Mass spectrometry (MS), 209, 219  
    commercial MS processing software, 86  
    compound identification, 86  
    fragmentation, 85, 86  
    high-resolution, 86  
    ionization, 84  
    LC-MS data, 86  
    low-resolution, 86  
    m/z values, 86  
    mass analyzers, 84  
    quadrupole analyzer, 85  
*Matricaria chamomilla*, 18–19  
*Maytenus ilicifolia*, 19, 20  
Medicinal plants, 2  
    pesticides, 4  
    principle, 3  
    synergism, 8  
    WHO, 26  
Medicinal teas, 5–6  
Medicines and Healthcare Products  
    Regulatory Agency (MHRA), 503  
Medium-pressure liquid chromatography (MPLC), 93  
Merilactone, 469  
Metabolic engineering, 37  
Metabolite profiling  
    biological activity, 87  
    chromatographic fingerprints  
        autoscaling, 89  
        column centering, 89  
        correlation graphics, 90  
        COW, 89  
        CV, 92  
        HCA, 90, 92  
        multivariate calibration, 91  
        PCA, 90, 91

peak alignment, 88  
PLS, 93  
pretreated, 88  
regression coefficients, 93  
RMSECV, 92  
supervised data analysis  
    techniques, 91  
    training set, 92  
unsupervised data analysis, 89  
UPLC-DAD, 89, 90  
warping, 89  
effect plots/effect fingerprints, 78  
Euclidean distance measurements, 77, 78  
*in vitro* enzymatic assays  
    BChE, 99, 100  
    MAO-A, 97, 99, 100  
    methanol-assisted micro-extraction, 99  
    *Morus alba*, 99, 101  
    OPLS, 99  
    *Pistacia atlantica*, 101  
    PLS, 99, 101  
*in vitro* reaction  
    antioxidant compounds, 96, 97  
    DPPH, 97  
    FRAP, 93, 94  
    HPLC fingerprint data, 94  
    LC-ESI-QToF-MS, 97  
    multivariate calibration, 97  
    OPLS regression modeling, 98  
    PFC, 97  
    PLS, 94, 95  
    regression coefficient profiles, 97  
    RMSEP, 95  
    SIS-iPLS, 96  
    synthetic sample set, 96  
    UV spectra, 94  
*in vivo* assays, 101–103  
pharmacological evaluation  
    extraction, 87  
    generic inactive extracts, 88  
    *in vitro* assays, 87, 88  
    *in vivo* assays, 88  
    LLE/SPE, 88  
    natural product, 87  
    phenols, 88  
    prefractionation, 87  
sample preparation  
    chemical analysis, 75  
    extraction, 75, 76  
    spectral techniques, 78  
    UPLC-DAD, 77  
    UV spectrum, 79  
Metabolites, 4  
Metabolomics, 218–220

- Methanol-assisted micro-extraction, 99
- Microbial-derived agents
- anthracyclines, 318–320
  - epothilones, 317, 318
  - staurosporin derivative, 316, 317
- Microencapsulation, 417, 438
- Microwave assisted extraction (MAE), 76
- application, 399–400
  - bioactive compounds, 396
  - biomolecules, 396
  - organic and organometallic compounds, 396
- Microwave-assisted intramolecular approach, 243
- Middle cerebral artery occlusion (MCAO), 175
- Minimum inhibitory concentration (MIC), 119
- Mitogen-activated protein kinases (MAPKs), 115, 169, 173
- Mode of action (MOA), 215
- Modular type I polyketide synthases (PKS-I), 289
- Molecular descriptors, 335, 337
- Molecular docking
- advantages, 341
  - AutoDock, 340
  - binding poses, 340, 341
  - Glide, 340
  - GOLD, 340
- Molecular dynamic (MD), 344, 345
- Molecular fingerprints, 338
- Monoamine oxidase-A inhibitory activity (MAO-A), 97, 99, 100
- Monographs
- herbal substances, 376–381
  - HMPC, 367, 375
  - and list entries, 370, 374
  - MLWP, 374
  - TCM, 367
  - traditional use, 371
  - usage and acceptance, 385
  - well-established use, 370, 371
- Morphine, 73
- Morus alba*, 99, 101, 355
- Multicomponent reactions (MCR)
- carbonyl allylboration, 244, 245
  - Diels-Alder cycloaddition, 244, 245
  - dihydropyran, 246
  - oxa [4+2] cycloaddition/allylboration, 245
  - (2*R*)-methoxy(phenyl)-acetaldehyde, 245, 246
  - thiomarinol, 246
- Multidimensional scaling, 214
- Multidisciplinary collaboration, 309
- Multivariate calibration, 91, 97
- Musella lasiocarpa*, 278
- Mutual Recognition Procedure (MRP), 368
- N**
- Nagoya Protocol, 36
- Nanodrug delivery, 403
- Nano drug delivery systems, 440
- Nanoprecipitation, 411, 415
- Nano phytomedicines, 440
- NAPRALERT database, 215
- Naproxen and dexamethasone, 25
- Naringenin (Nar), 182
- Naringin (Nag), 183
- National Center for Complementary and Alternative Medicine (NCCAM), 496
- National Center for Complementary and Integrative Health (NCCIH), 508
- National Health Systems (NHS), 497
- National Policy on Complementary and Integrative Practices (PNPIC), 504
- National Policy on Medicinal Plants and Herbal Medicines (PNPMF), 504
- National procedure, 369
- Natural and Non-prescription Health Products Directorate (NNHPD), 508
- Natural health products (NHPs), 508
- Natural Health Products Directorate (NHPD), 508
- Natural product (NP)
- artemisinin, 74
  - anticancer agents, 309
  - antitumor activity (*see* Antitumor agents)
  - auxiliary arms, 210
  - bioactivity-guided fractionation, 74
  - compound activity mapping, 212
  - drug discovery, 209, 210
  - 4*H*-chromenes, 253
  - hit-identification strategy, 211
  - $\alpha$ -hydroxyalkyl pyrans, 245
  - isolation and chemical structure elucidation, 223–227
  - metabolomic profiling and dereplication, 210
  - microbial-derived agents, 317
- NMR
- active nuclei, 466
  - dinimbiol ether, 467, 468
  - epi-flemistricin B*, 466, 467
  - <sup>1</sup>H-NMR, 466
  - merilactone, 469

- 3-*o*-acetyl ceanothoic acid, 467
    - structural features, 466
  - organic chemistry, 209
  - organocatalytic oxa-Michael reaction, 253, 254
  - PM0500489 and PM060184, 213
  - polycyclic xanthone, 251
  - quantitative dataset analysis, 211
  - six membered oxygen heterocycles (*see* Six membered oxygen heterocycles)
  - warhead
    - calicheamicin, 326
    - camptothecin-derived, 327
    - dolastatin-derived, 325
    - duocarmycin-derived, 326
    - maytansine-derived, 325
    - PBD-derived, 327
    - structures, 324
    - tubulysin-derived, 327
  - Neural network technique, 349
  - Niosomes, 424
    - formulations, 425–428
    - phytosomal, 431–433
    - preparation, 429–430
    - properties, 429
    - structure, 429
  - Nitric oxide (NO), 168
  - Nitric oxide synthase (NOS), 168
  - Nitrosamines, 137
  - Nitrosugars, 243
  - Non-steroidal anti-inflammatory drugs (NSAIDs), 168
  - Nontraditional medical profession, 511
  - Nozaki-Hiyama-Kishi procedure, 288
  - Nuclear factor kappa B (NF- $\kappa$ B), 115, 167
  - Nuclear magnetic resonance (NMR), 84, 209, 219
    - $^{13}\text{C}$  (*see*  $^{13}\text{C}$ -NMR)
    - $^1\text{H}$  (*see*  $^1\text{H}$ -NMR)
    - absorption of energy, 465
    - flavonoids (*see* Flavonoids)
    - J*-resolved, 485
  - NP
    - $^1\text{H}$ -NMR, 466
    - 3-*O*-acetyl ceanothoic acid, 467
    - active nuclei, 466
    - dinimbiol ether, 467, 468
    - epi-flemistricin B*, 466, 467
    - merilactone, 469
    - structural features, 466
  - split peaks, 465
  - terpenoids
    - Ent*-kaurenes, 474, 475
    - pregnanes, 476, 477
    - urechitol A, 470, 472, 473
  - Nuclear Overhauser Effect (NOE), 482
  - Nuclear transcription factor kappa-B (NF- $\kappa$ B), 171, 172
  - Nucleoside-derived agents
    - acelarin, 321
    - guadecitabine, 322
    - microbes, 320
    - namodenoson, 322
    - sapacitabine, 320
    - uridine triacetate, 320
- O**
- Olea europaea* L., *see* Olive oil
  - Oleuropein, 125–127
  - Olive oil
    - aliphatic alcohols, 124
    - antioxidant activity, 125
    - bioactive compounds, 126
    - chemical composition, 123
    - factors, 123
    - flavonoids, 124
    - glucuronides, 125
    - hydrocarbons, 124
    - metastatic process, 127
    - nutrients and non-nutrients, 123
    - oleuropein, 126
    - polar and lipophilic phenolic compounds, 124
    - secoiridoids, 125
    - sensory characteristics, 123
    - sterols, 124
    - triacylglycerols, 123
  - Omega-3 ( $\omega$ -3/n-3), 120–123
  - Ononin (Ono), 190
  - Ordinary matter, 213
  - Organizational Matters Drafting Group (ORGAM DG), 373
  - Organocatalytic oxa-Michael reaction, 253, 254
  - Oroxilin A (OroA), 178
  - Orthogonal Partial Least Square - Discriminant Analysis (OPLS-DA), 102
  - Oxa-cyclization method, 256
  - Oxa [4+2] cycloaddition/allylboration, 245
  - Oxa-Michael reaction, 255, 258
  - Oxygen heterocycles, 233
  - Ozonolysis, 295
- P**
- Paeoveitol, 241, 242

- Pan Assay Interference Compounds (PAINS), 87
- Parametric Time Warping (PTW), 89
- Peak-splitting, 465
- Pelargonidin (Pel), 188
- Pelargonidin-3-glucoside (P3G), 188
- Pentalinon andrieuxii*, 470, 476
- Peonidin (Peo), 188
- Peruvian medicinal plants, 6, 7
- Pesticides, 4
- Pharmacophore
- advantages, 344
  - definition, 341
  - interaction types, 341
  - ligand-based, 342
  - RDF, 343
  - scaffold-hopping, 344
  - target-based, 342
- Phase I deglycosylation, 165
- Phenolic compounds, 41
- Phenols, 88
- Phloretin (Phl), 191
- Phlorizin
- dapagliflozin, 265
  - diabetes mellitus, 263
  - pharmacology, 263
  - salt formation, 263
- Phosphatidylinositol-3 kinase (PI3K), 169
- Phosphoenolpyruvate carboxykinase (PEPCK), 129
- Phyllanthus engleri*, 276
- Phyllanthus niruri*, 23
- Phytomedicines, 36
- Allium sativum*, 15
  - biodiversity, 24–26
  - chamomile, 18
  - Cynara scolymus*, 21
  - definition, 2
  - ESI-MS and LC-MS methods, 3
  - Ginkgo biloba*, 11
  - Glycine max, 17–18
  - herbal products, 9
  - Hypericum perforatum*, 13
  - Ilex paraguariensis*, 20
  - intoxication, 4
  - liquid, 5
  - Maytenus ilicifolia*, 19
  - pharmacological qualities, 3
  - Phyllanthus niruri*, 23
  - phytotherapeutics, 3
  - phytotherapy, 3
  - Piper methysticum*, 16
  - preparations, 4
  - Serenoa repens*, 11
  - valerian, 13
- Phytopharmaceuticals research, 393
- Phytosomes®, 440
- Phytotherapy, 3, 497, 498
- biological screening, 6
  - DNA elements, 7
  - drug resistance, 7
  - NF-κB/DNA interactions, 7
  - phytopharmaceuticals, 6
  - synergy, 9
- Pinocembrin (Pin), 184
- Piper methysticum*, 16, 17
- Piper nigrum* Linn, 134
- Piperine, 135
- Pistacia atlantica*, 101
- Plant bioactive compounds, 47, 394
- Plant cultivation, 56
- Plant extracts conservation, 392
- Plant organ cultures, 60–62
- Plants extracts, 409
- Polychlorinated biphenyls (PCBs), 186
- Polycyclic xanthone, 251, 252
- Polyethylene glycol (PEG), 411
- Polymeric nanoparticles, 410
- Polymer selection criteria, 408
- Prebiotics, 143–145
- Pressurized fluid extraction (PFE)
- application, 402
  - flavonoids, 400
  - optimum condition, 400
  - PLE, 400
- Pressurized solvent extraction (PSE), 76
- Primary health care, 498
- Principal component analysis (PCA), 90, 91
- chromatographic fingerprints, 91
  - goodness of fit and predictability, 102
  - UHPLC, 103
  - variable reduction, 90
- Principium somniferum*, 73
- Probiotics
- butyric acid, 137
  - dietary supplements, 137
  - enterocytes, 137
  - gut microbiota, 137
  - intestinal epithelial cells, 136
  - kefir, 140, 141
  - Kombucha, 142, 143
  - microorganisms, 137
  - nutritional and therapeutic function, 136
  - phytochemicals, 138
  - SCFA, 137
  - yogurt, 138, 139

Protein Data Bank (PDB), 344  
Protein kinase C (PKC), 289  
Prunetin (Pru), 190  
PubChem BioAssay database, 214  
Public scrutiny, 511  
Puerarin (Pue), 189  
*Punica granatum*, 42  
Pyran-containing natural product (PCNP)  
  and carbohydrates, 234  
  biological diversity, 234  
  glycosylated form, 234, 235  
  non-sugar, 234  
Pyran derivatives  
  KDO (*see* 3-Deoxy-D-manno-  
    2-octulosonic acid (KDO))  
Pyranosulose lactols and lactones, 276  
Pyridinium p-toluenesulfonate (PPTS), 295

## Q

Quadrupole mass analyzers, 85  
Quality assurance system, 506  
Quality control (QC), 500  
Quality Drafting Group (Q DG), 373  
Quantitative structure activity relationship  
  (QSAR), 337  
Quercetin-lipid nanoformulations, 440  
Query pharmacophore models, 342  
Quinic acid esters, 490, 491  
Quinocinnolinomycins, 212

## R

Radial distribution function (RDF), 343  
Reactive oxygen species (ROS), 120  
Regulated upon activation normal T-cell  
  expressed and secreted (RANTES),  
  186  
Regulatory framework, 367, 383, 387  
Resveratrol, 134  
Ring-closing metathesis (RCM)  
  chiral olefins, 248  
  dihydropyrans, 248  
  halichondrin B subunit, 250  
  2*H*-chromenes, 250, 251  
  2*H* Pyrans, 249  
   $\delta$ -lactones, 250  
  lactones, 249  
  malyngolide, 249  
  NaH/NaBH<sub>4</sub>, 248  
  polycyclic ethers, 249  
  vinyl ethers, 248

Root mean squared error of cross validation  
  (RMSECV), 92, 97  
Root Mean Squared Error of Prediction  
  (RMSEP), 95  
Ru-based dithiolate catalysts, 248  
Ruthenium-based metathesis catalysts, 247  
Rutin (Rut), 179

## S

Safety, 383  
Saw palmetto, 11  
Scaffold-hopping, 344, 346  
Scatterplot (S-plot), 102  
Secondary metabolites, 56, 60, 393  
*Serenoa repens*  
  BPH, 12  
Shape-based screening, 345, 346  
Sharpless asymmetric dihydroxylation, 292  
Shogaols, 131  
Short chain fatty acids (SCFA), 137  
Signal transducer and activator of transcription  
  (STAT), 169, 171, 172  
Sirtuins, 116  
Six membered oxygen heterocycles  
  biological activity, 235  
  HDA reaction  
    and aldehydes, 236  
    catalyst-controlled doubly  
      diastereoselective, 238  
    chiral substrate control, 237  
    Danishefsky's diene, 238, 239  
    dihydropyranone stereoisomers, 237  
    dihydropyrans, 236  
    2*H*-pyrans, 236  
    (salen)Cr(III)-BF<sub>4</sub> complex, 237  
    structural heterocyclic core, 236  
    substrate-controlled  
      diastereoselective, 237  
Skimmiwallin, 478, 480  
Skin mycoses, 35  
Skin-related infections, 35  
Small Molecule Accurate Recognition  
  Technology (SMART), 222, 224  
Sol-gel encapsulation, 434  
Solid lipid nanoparticles (SLNs), 430  
Solid-liquid extraction method, 225  
Solid-phase extraction (SPE), 76  
Solvent evaporation, 417  
Sophoraflavanone G (SG), 184  
Spectral techniques, 78  
Spectroscopic detection, 83, 84  
Spray drying, 435

- Staurosporin derivative, 316, 317  
*Stevia rebaudiana*, 62  
 Structural elucidation, 217–220, 228  
 Structure elucidation  
<sup>13</sup>C-NMR, 488  
 lupeol-3-(3'-R-hydroxy)-stearate, 488  
 NMR (*see* Nuclear magnetic resonance (NMR))
- Sugars  
 organic synthesis, 233  
 oxygen heterocyclic, 233
- Sulforaphane, 133  
 Sulfotransferases (SULTs), 165  
 Supercritical fluid extraction (SFE), 5, 76–78  
 antioxidants, 403  
 application, 404–407  
 polyphenols and procyanidins, 402  
 properties, 401
- Superficial mycoses, 38  
 Supervised data analysis techniques, 91  
 Sure Independence Screening interval PLS (SIS-iPLS), 94, 96
- Synbiotics, 145  
 Synergism, 8  
 Synergism  
 and antagonism, 9
- T**
- Tanimoto coefficient (TC), 339  
 Tannin punicalagin, 42  
 Target Interference Generator (TIGER), 356  
 Taxifolin (Tax), 185  
 Taxol derivatives, 314, 315
- Tea  
 caffeine and L-theanine, 130  
*Camellia sinensis*, 127  
 catechins, 128  
 cellular enzymes, 129  
 DM, 129  
 EGCG, 127, 129  
 flavonoids, 127  
 green tea consumption, 129  
 harvested leaf development, 127  
*in vivo and in vitro studies*, 128  
 neuroprotective/neurorestorative action, 130  
 oxidative stress, 129  
 polyphenols, 130
- Tea fungus, 142  
 Terpenoids  
*Ent*-kaurenes, 474, 475  
 pregnanes, 476
- Tetrahydropyran (THP) rings, 288
- Therapeutic potential, 17, 23  
 Thin-Layer Chromatography (TLC), 79, 80  
 Thiomarinol, 246  
 Time-of-Flight mass analyzer, 85  
 Tofogliflozin, 268  
 Toll-like receptor 4 (TLR4), 167  
 Total Correlation Spectroscopy (TOCSY), 485  
 Traditional Arabic and Islamic Medicine (TAIM), 507  
 Traditional Chinese medicine (TCM), 496, 505  
 monographs, 367  
 Traditional herbal medicinal product (THMP), 367, 499, 507  
 Traditional Korean medicine (TKM), 496  
 Traditional medicine (TM), 496  
 Traditional Medicine Practice Act, 506  
 Traditional medicine practitioners (TMP), 503, 504  
 Traditional medicines  
 Asian, 367  
 globalization, 366  
 regulatory framework, 387
- Triacylglycerols (TAG), 122  
 Tricin (Tri), 178  
 Tumor necrosis factor alpha (TNF- $\alpha$ ), 167
- Turmeric  
 antioxidant proteins, 115  
 apoptosis, 116  
 cancer types, 117  
 chemical structures, 114  
 cytoprotective proteins, 115  
 diferuloylmethane, 115  
 encapsulation, 117  
 functional groups, 115  
 HDL and LDL, 117  
 inflammatory cytokines, 116  
 malignant diseases, 115  
 miRNAs, 116  
 phytochemicals, 116  
 protein kinases, 115  
 rhizome, 114  
 Zingiberaceae family, 113
- Tyrosol, 126
- U**
- Ugonin M (UgoM), 184  
 UHPLC-QToF-MS, 101  
 UHPLC-UV-MS-SPE-NMR system, 225  
 Ultra High Pressure Liquid Chromatography (UHPLC), 83, 102, 103  
 Ultrasound assisted extraction (UAE), 76  
 application, 397–398

- benefit, 395
  - isoflavones, 396
  - polyphenol, 396
  - Unilateral ureteral obstruction mice model, 186
  - Unsupervised data analysis, 89
  - Urechitol A
    - 13C-NMR, 470, 472
    - COSY, 471
    - HMBC, 473
    - <sup>1</sup>H-NMR, 471
    - HSQC, 472
    - <sup>2</sup>J correlation, 473
    - <sup>3</sup>J correlation, 473
    - single-crystal X-ray diffraction, 474
  - Uridine 5'-diphospho-glucuronosyltransferases (UGTs), 165
  - U.S. Department of Health and Human Services and Agriculture (USDHHS/USDA), 122
- V**
- Valeriana officinalis*, 13, 14
    - GABA, 13
    - principles, 13, 14
  - Vascular endothelial growth factor (VEGF), 177
  - Vascular-cell adhesion molecule (VCAM-1), 170
  - Velutin (Vel), 177
  - Viequeamide A, 223
  - Vinca alkaloid derivatives, 310–312
  - Virtual screening (VS)
    - definition, 339, 340
    - herbal remedies, 346
    - limitations and caveats
      - 3D methods, 350
      - hit identification criteria, 351
      - in silico* experiment, 349
      - inactive molecules, 349
      - ligand-based, 350
      - performances and comparison, 350
    - machine learning, 348
    - MD, 344, 345
    - molecular docking, 340, 341
    - NP
      - hitlist, 352, 353
      - molecular binding mechanism, 356
      - molecular targets, 355, 356
      - quality and availability, resources, 351, 352
      - selection of compounds, 354, 355
    - pharmacophore
      - ligand-based, 343, 344
      - target based, 341
      - target-based, 342
    - polypharmacological profiling, 347
    - prerequisites, 347
    - shape-based screening, 345, 346
    - side effects, 347
    - virtual target fishing, 346, 348
  - Vitamin P, 163
  - Vitexin (Vix), 176
  - Vitis vinifera*, 134
- W**
- Warhead
    - calicheamicin, 326
    - camptothecin-derived, 327
    - dolastatin-derived, 325
    - duocarmycin-derived, 326
    - maytansine-derived, 325
    - PBD-derived, 327
    - structures, 324
    - tubulysin-derived, 327
  - Wogonin (Won), 176
  - Woody plants, 56
  - Working Party on Monographs and List Entries (MLWP), 374
  - World Health Organization (WHO), 496
- Y**
- Yogurt, 138, 139
- Z**
- Zebra fish models
    - embryos, 102
    - fingerprints, 102
    - PCA score plot, 102
    - SIVs, 102
  - Zingiber officinale*, 130