

Contents

1. Introduction	17
Definitions	17
The history of natural products in medicine	17
Natural products as modern drugs	19
Production of drugs based on natural products	20
The role of natural products in drug discovery	21
Plants used in traditional medicine.	
Ethnopharmacology	22
Natural products from marine organisms	24
Combinatorial biosynthesis	27
Screening of randomly chosen organisms	28
Cheminformatics and phylogenetics	28
Systems biology	31
Application of the systemic biology approach to the study of natural products used in medicine	33
Pharmacognosy as a research subject	37
Further reading	41
2. Plant derived Crude drugs and Herbal Remedies	45
Nomenclature	45
Production of crude drugs from medicinal plants	47
Cultivation of medicinal plants	48
Propagation of plants	51
Plant breeding	52
Collecting and harvesting medicinal plants	56
Preservation of plant material	57
Storage of crude drugs	59
Quality control of crude drugs	60
Sterilization of crude drugs	64
Preparations of crude drugs	65
Grinding of crude drugs	65
Herbal “Teas”	67
Extracts	68
Herbal remedies	78
Definitions and trade regulations	78
Side effects	80
Interactions	81
Information sources	81
Isolation of pure compounds from extracts of crude drugs and other organisms	81
Isolation of compounds with known properties	81
Bioassay-guided isolation	83
Industrial high-throughput screening of extracts	86
Further reading	87

3. Biotechnological Drug Production	89
Production of Antibiotics	89
The growth curve of microorganisms	90
Energy metabolism and production of metabolites in microorganisms	92
Technical aspects on the production of antibiotics ..	93
Plant tissue and cell culture (Plant Biotechnology)	96
Callus cultures	96
Suspension cultures	98
Organ cultures and regeneration of plants	99
Environmental factors of importance for plant tissue and cell culture	99
Tissue and cell culture in plant breeding	101
Industrial production of natural products by plant tissue and cell cultures	105
Future prospects for plant biotechnology in the production of drugs	109
Further reading	112
4. Formation of Pharmacologically Active Compounds in Plants – Biosynthesis	114
Photosynthesis	114
Light reactions and dark reactions	116
Dark reactions	128
Photorespiration	131
C ₃ Plants	131
CAM and C ₄ plants	132
Biosynthetic pathways	134
Glycolysis and the citric acid cycle	136
Investigation of biosynthetic pathways	139
Transporters of secondary metabolites	145
Classification of natural products	146
Further reading	146
5. Carbohydrates	148
Monosaccharides	148
Disaccharides	150
Polysaccharides	153
Gums and mucilages	169
Reduction products of carbohydrates: sugar alcohols ..	175
Natural products related to carbohydrates	176
Glycosides	179
Aminoglycoside antibiotics	181
Acarbose	189
Ethyl alcohol, C ₂ H ₅ OH	191
Further reading	192

6. Natural Products Derived Biosynthetically from Shikimic Acid	194
Shikimic acid	194
Localization of the shikimic acid pathway	195
The enzymes of the shikimic acid pathway	195
Biosynthesis of shikimic acid	196
Gallic acid and tannins	199
The aromatic amino acids phenylalanine, tyrosine and tryptophan	202
Biosynthesis of tyrosine and phenylalanine	204
Biosynthesis of tryptophan	206
Phenylpropanes	208
Typical phenylpropanes	208
Adaptogens	226
Coumarins and furanocoumarins	228
Substances formed from phenylpropanes by shortening of the side-chain	232
Further reading	235
7. Natural Products Derived Biosynthetically from Acetate	237
7a. The acylpolymalonate pathway	237
Fatty acids	238
Saturated fatty acids	238
Unsaturated fatty acids	247
Other derivatives of fatty acids	248
Fats and waxes	249
Fats	249
Waxes	255
Phospholipids	256
Eicasonoids	256
Prostaglandins	256
Thromboxanes	262
Leukotrienes	263
Lipstatin	266
Polyketides	266
Polyketides derived from acetate or propionate	271
Macrolides	271
Erythromycins	272
Avermectins	278
Spiramycins	283
Polyene macrolide antibiotics	283
Epothilones	291
Griseofulvin	292
Aflatoxins	292
Mevastatin and lovastatin	297
Leptospermone and Nitisinone	300
Mupirocin	301
Tetracyclines	303

Anthracyclines	305
Enediynes	307
Anthraquinones	312
Polyketides of mixed biogenetic origin	328
Flavonoids	329
Kava pyrones	337
Flavonolignans	339
Mycophenolic acid	340
The ansamycin group of antibiotics	342
Rapamycin	347
Tacrolimus (FK-506)	349
Rotenoids	352
Khellin	355
Sodium cromoglycate	356
Further reading	358
7b. The isopentenyl diphosphate pathway Isoprenoids	366
Mevalonic acid and isopentenyl diphosphate	367
The non-mevalonate pathway for the biosynthesis of isoprenoids	369
Monoterpenes	372
Biosynthesis of monoterpenes	372
Hydrocarbons	375
Alcohols	376
Aldehydes	380
Ketones	381
Phenols	381
Iridoids and secoiridoids	382
Other oxidized monoterpenes	390
Sesquiterpenes	400
Biosynthesis of sesquiterpenes	400
Diterpenes	413
Biosynthesis of diterpenes	413
Triterpenes and steroids	434
Biosynthesis of triterpenes and steroids	434
Biosynthesis of pentacyclic triterpenes	436
Biosynthesis of tetracyclic triterpenes and steroids	438
Triterpenes	439
Saponins	440
Modified triterpenes	448
Steroidal hormones	449
Cardiac glycosides	459
Glycosides from <i>Digitalis purpurea</i>	461
Glycosides from <i>Digitalis lananta</i>	468
Other cardiac glycosides	470
Vitamin D	473
Tetraterpenes	474
Biosynthesis of tetraterpenes	475
Further reading	479

8. Amino acids	486
2-oxoglutaric acid group	487
Pyruvic acid group	491
Oxalacetic acid group	493
Serine group	499
Histidine	503
Aromatic amino acids	505
Essential amino acids	505
Toxic, non-proteinogenic amino acids	505
Further reading	507
9. Natural Products Derived Biosynthetically from Amino Acids	509
Peptides and proteins	509
Symbols for the amino acids in primary structures of peptides and proteins	509
Proteolytic enzymes	510
Ribosome inactivating proteins (RIP toxins)	513
Lectins	518
Amanita toxins	519
Snake venoms	522
Lizard toxins	525
Ziconotide	526
Mistletoe toxins	527
Cyclotides	529
Non-ribosomal polypeptides	531
Glycopeptide antibiotics	547
Streptogramin antibiotics	553
β -Lactam antibiotics	560
Other β -lactams	571
Vitamines derived from amino acids	573
Cyanogenic glycosides	588
Glucosinolates (mustard-oil glycosides)	594
Further reading	597
10. Alkaloids	604
General aspects	604
Amino alkaloids	609
Pyridine and piperidine alkaloids	622
Tropane alkaloids	630
Pyrrolizidine alkaloids (<i>Senecio</i> alkaloids)	640
Quinolizidine alkaloids (<i>Lupinus</i> alkaloids)	642
Isoquinoline alkaloids	644
Protoberberine alkaloids	645
Benzylisoquinoline alkaloids	648
Bisbenzylisoquinoline alkaloids	661
Amaryllidaceae alkaloids	663
Benzophenanthridine alkaloids	665
Terpenoid tetrahydroisoquinoline alkaloids	667

Indole alkaloids	668
Simple indole alkaloids	669
Terpenoid indole alkaloids	672
Quinoline alkaloids	692
Imidazole alkaloids	699
Steroidal alkaloids	699
Aconitum alkaloids	704
Guanidinium alkaloids	705
Further reading	706
11. Purines and Pyrimidines	712
Purine derivatives	712
Biosynthesis	712
ATP	715
Nicotinamide adenine dinucleotide (NAD ⁺) and nicotinamide adenine dinucleotide phosphate (NADP ⁺)	716
Coenzyme A (CoA)	720
Guanosine 5'-triphosphate (GTP)	722
Riboflavin	722
Flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD)	724
5,6,7,8-Tetrahydrofolate (THF, Vitamin B ₉)	725
Caffeine, theobromine and theophylline	729
Pyrimidine derivatives	737
Uridine triphosphate (UTP)	738
Cytidine triphosphate (CTP)	739
Cytarabine (Ara-C)	740
Thiamin (Vitamin B ₁)	741
Further reading	745
Appendix I	748
Index	750