

Contents

1. Introduction	19
Definitions	19
The history of natural products in medicine.....	19
Natural products as modern drugs.....	21
Production of drugs based on natural products	22
The role of natural products in drug discovery	23
Plants used in traditional medicine	
Ethnopharmacology	24
Natural products from marine organisms	26
Combinatorial biosynthesis.....	29
Screening of randomly chosen organisms	30
Chemoinformatics and phylogenetics.....	30
Systems biology	33
Application of the systemic biology approach to the study of natural products used in medicine.....	35
Pharmacognosy as a research subject.....	40
Further reading	44
2. Plant- derived Crude Drugs and Herbal Remedies	48
Nomenclature	48
Production of crude drugs from medicinal plants	50
Cultivation of medicinal plants.....	51
Propagation of plants	53
Plant breeding	55
Collecting and harvesting medicinal plants	59
Preservation of plant material	60
Storage of crude drugs	62
Quality control of crude drugs	62
Sterilization of crude drugs.....	67
Preparations of crude drugs	67
Grinding of crude drugs.....	68
Herbal “Teas”	70
Extracts	71
Herbal remedies.....	80
Definitions and trade regulations	80
Side effects.....	83
Interactions.....	83
Information sources	84
Isolation of pure compounds from extracts of crude drugs and other organisms.....	84
Isolation of compounds with known properties.....	84
Bioassay-guided isolation	86
Industrial high-throughput screening of extracts	89
Further reading	90

3. Biotechnological Drug Production	92
Production of antibiotics	92
The growth curve of microorganisms.....	93
Energy metabolism and production of metabolites in microorganisms.....	95
Technical aspects of the producton of antibiotics.....	96
Plant tissue and cell culture (plant biotechnology)	99
Callus cultures.....	99
Suspension cultures.....	101
Organ cultures and regeneration of plants	102
Environmental factors of importance for plant tissue and cell culture.....	102
Tissue and cell culture in plant breeding	104
Industrial production of natural products by plant tissue and cell cultures	108
Future prospects for plant biotechnology in the production of drugs	112
Further reading	115
4. Formation of Pharmacologically Active Compounds in Plants – Biosynthesis	117
Photosynthesis	117
Light reactions and dark reactions	119
Dark reactions	131
Photorespiration	134
C ₃ Plants.....	134
CAM and C ₄ plants	135
Biosynthetic pathways.....	137
Glycolysis and the citric acid cycle	139
Investigation of biosynthetic pathways.....	142
Transporters of secondary metabolites	151
Classification of natural products	152
Further reading	152
5. Carbohydrates	154
Monosaccharides	154
Disaccharides.....	156
Polysaccharides	159
Gums and mucilages.....	169
Reduction products of carbohydrates:	
sugar alcohols	175
Natural products related to carbohydrates.....	176
Glycosides	180
Aminoglycoside antibiotics.....	182
Acarbose.....	190
Ethyl alcohol, C ₂ H ₅ OH	193
Further reading	194

Anthracyclines	307
Mithramycin.....	309
Enediynes.....	311
Anthraquinones.....	315
Polyketides of mixed biogenetic origin.....	332
Flavonoids.....	333
Kava pyrones	341
Flavonolignans.....	343
Mycophenolic acid.....	344
The ansamycin group of antibiotics.....	346
Rapamycin	352
Tacrolimus (FK-506)	356
Rotenoids	359
Khellin	361
Sodium cromoglycate	362
Further reading	364

7b. The isopentenyl diphosphate pathway

Isoprenoids	375
Mevalonic acid and isopentenyl diphosphate	376
The non-mevalonate pathway for the biosynthesis of isoprenoids	379
Monoterpenes	381
Biosynthesis of monoterpenes	382
Hydrocarbons.....	384
Alcohols	385
Aldehydes	389
Ketones	390
Phenols.....	390
Iridoids and secoiridoids.....	391
Other oxidized monoterpenes	398
Sesquiterpenes	408
Biosynthesis of sesquiterpenes	408
Diterpenes.....	423
Biosynthesis of diterpenes	423
Triterpenes and steroids.....	445
Biosynthesis of triterpenes and steroids.....	445
Biosynthesis of pentacyclic triterpenes.....	447
Biosynthesis of tetracyclic triterpenes and steroids..	449
Triterpenes	450
Saponins.....	451
Modified triterpenes.....	460
Steroidal hormones	461
Cardiac glycosides	471
Glycosides from <i>Digitalis purpurea</i>	473
Glycosides from <i>Digitalis lananta</i>	480
Other cardiac glycosides.....	482
Vitamin D.....	485
Tetraterpenes	486

6. Natural Products Derived Biosynthetically from Shikimic Acid	196
Shikimic acid.....	196
Localization of the shikimic acid pathway	197
The enzymes of the shikimic acid pathway	197
Biosynthesis of shikimic acid	198
Gallic acid and tannins	201
The aromatic amino acids phenylalanine, tyrosine and tryptophan.....	204
Biosynthesis of tyrosine and phenylalanine.....	206
Biosynthesis of tryptophan	208
Phenylpropanes	210
Typical phenylpropanes	210
Adaptogens	229
Coumarins and furanocoumarins	231
Substances formed from phenylpropanes by shortening of the side-chain.....	235
Further reading	238
7. Natural Products Derived Biosynthetically from Acetate	240
7a. The acylpolymalonate pathway	240
Fatty acids	241
Saturated fatty acids.....	241
Unsaturated fatty acids.....	250
Other derivatives of fatty acids.....	251
Fats and waxes	252
Fats.....	252
Waxes.....	258
Phospholipids	258
Eicasonoids.....	259
Prostaglandins.....	259
Thromboxanes	265
Leukotrienes.....	266
Lipstatin	269
Polyketides	269
Polyketides derived from acetate or propionate	275
Macrolides	275
Erythromycins.....	275
Avermectins	281
Spiramycins	281
Polyene macrolide antibiotics.....	286
Epothilones	294
Polyether macrolides	295
Griseofulvin	296
Mevastatin and lovastatin	298
Leptospermone and Nitisinone	301
Mupirocin.....	302
Tetracyclines	303

Bisbenzylisoquinoline alkaloids	686
Amaryllidaceae alkaloids	688
Benzophenanthridine alkaloids	690
Terpenoid tetrahydroisoquinoline alkaloids	692
Indole alkaloids	693
Simple indole alkaloids.....	694
Terpenoid indole alkaloids.....	697
Quinoline alkaloids	717
Imidazole alkaloids.....	724
Steroidal alkaloids	724
Aconitum alkaloids	729
Guanidinium alkaloids	730
Further reading	732
11. Purines and Pyrimidines.....	739
Purine derivatives	739
Biosynthesis	739
ATP	742
Nicotinamide adenine dinucleotide (NAD ⁺) and nicotinamide adenine dinucleotide phosphate (NADP ⁺)	744
Coenzyme A (CoA).....	748
Guanosine 5'-triphosphate (GTP).....	750
Riboflavin.....	750
Flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD).....	752
5,6,7,8-Tetrahydrofolate (THF, Vitamin B ₉).....	753
Caffeine, theobromine and theophylline.....	758
Pyrimidine derivatives.....	765
Uridine triphosphate (UTP)	766
Cytidine triphosphate (CTP).....	767
Cytarabine (Ara-C)	768
Thiamin (Vitamin B ₁)	769
Further reading	773
12. Phosphonates and phosphinates	776
Appendix I	778
Index.....	780

	Biosynthesis of tetraterpenes	487
	Further reading	491
8.	Amino acids	500
	2-oxoglutaric acid group	501
	Pyruvic acid group	505
	Oxalacetic acid group	507
	Serine group	513
	Histidine	517
	Aromatic amino acids	519
	Essential amino acids	519
	Toxic, non-proteinogenic amino acids	519
	Other amino acids of medicinal interest	521
	Further reading	523
9.	Natural Products Derived Biosynthetically from Amino Acids	524
	Peptides and proteins	524
	Symbols for the amino acids in the primary structures of peptides and proteins	524
	Proteolytic enzymes	525
	Other enzymes with medicinal use	528
	Ribosome inactivating proteins (RIP toxins)	528
	Lectins	534
	Amanita toxins	535
	Snake venoms	538
	Lizard toxins	541
	Ziconotide	543
	Mistletoe toxins	543
	Cyclotides	545
	Non-ribosomal polypeptides	548
	Glycopeptide antibiotics	567
	Streptogramin antibiotics	574
	β -Lactam antibiotics	581
	Other β -lactams	593
	Vitamins derived from amino acids	598
	Further reading	616
10.	Alkaloids	625
	General aspects	625
	Amino alkaloids	630
	Aziridine alkaloids	643
	Pyridine and piperidine alkaloids	645
	Tropane alkaloids	653
	Pyrrolizidine alkaloids (<i>Senecio</i> alkaloids)	664
	Quinolizidine alkaloids (<i>Lupinus</i> alkaloids)	666
	Isoquinoline alkaloids	668
	Protoberberine alkaloids	669
	Benzylisoquinoline alkaloids	672