

Contents

Preface xv

Part I General Aspects of Nucleotide Metabolism 1

1	Structures of Nucleotide-Related Compounds	3
1.1	Introduction	3
1.2	Nomenclature and Abbreviations of Nucleotide-Related Compounds	3
1.3	Chemical Structures of Nucleotide-Related Compounds	5
1.3.1	Purines	5
1.3.1.1	Purine Bases	5
1.3.1.2	Purine Nucleosides	6
1.3.1.3	Purine Nucleotides	7
1.3.2	Pyrimidines	8
1.3.2.1	Pyrimidine Bases	9
1.3.2.2	Pyrimidine Nucleosides	9
1.3.2.3	Pyrimidine Nucleotides	10
1.3.3	Pyridines	11
1.4	Summary	11
	References	11
2	Occurrence of Nucleotides and Related Metabolites in Plants	13
2.1	Purines and Pyrimidines	13
2.1.1	Concentration of Purine and Pyrimidine Nucleotides	14
2.1.2	Concentration of Purine and Pyrimidine Bases and Nucleosides	16
2.2	Pyridine Nucleotides	17
2.2.1	Concentration of Pyridine Nucleotides	17
2.2.2	Concentration of Nicotinate and Nicotinamide	18
2.3	Concentration of Cytokinins	18
2.4	Alkaloids Derived from Nucleotides	18
2.5	Summary	19
	References	19
3	General Aspects of Nucleotide Biosynthesis and Interconversions	21
3.1	Introduction	21
3.2	<i>De Novo</i> Biosynthesis of Ribonucleoside Monophosphates	21

3.3	Interconversion of Nucleoside Monophosphates, Nucleoside Diphosphates, and Triphosphates	23
3.3.1	Nucleoside-Monophosphate Kinase	23
3.3.2	Specific Nucleoside-Monophosphate Kinases	24
3.4	Conversion of Nucleoside Diphosphates to Nucleoside Triphosphates	24
3.4.1	ATP Synthesis by Electron Transfer Systems	25
3.4.2	Substrate-Level ATP Synthesis	26
3.4.3	Nucleoside-Diphosphate Kinase	26
3.5	Biosynthesis of Deoxyribonucleotides	29
3.6	Nucleic Acid Biosynthesis	29
3.7	Supply of 5-Phosphoribosyl-1-Pyrophosphate	30
3.8	Supply of Amino Acids for Nucleotide Biosynthesis	33
3.9	Nitrogen Metabolism and Amino Acid Biosynthesis in Plants	33
3.10	Summary	34
	References	35

Part II Purine Nucleotide Metabolism 39

4	Purine Nucleotide Biosynthesis <i>De Novo</i>	41
4.1	Introduction	41
4.2	Reactions and Enzymes	43
4.2.1	Synthesis of Phosphoribosylamine	44
4.2.2	Synthesis of Glycineamide Ribonucleotide	46
4.2.3	Synthesis of Formylglycineamide Ribonucleotide	46
4.2.4	Synthesis of Formylglycinamide Ribonucleotide	47
4.2.5	Synthesis of Aminoimidazole Ribonucleotide	47
4.2.6	Synthesis of Aminoimidazole Carboxylate Ribonucleotide	48
4.2.7	Synthesis of Aminoimidazole Succinocarboxamide Ribonucleotide	48
4.2.8	Synthesis of Aminoimidazole Carboxamide Ribonucleotide	49
4.2.9	Synthesis of IMP via Formamidoimidazole Carboxamide Ribonucleotide	49
4.2.10	Synthesis of AMP	50
4.2.11	Synthesis of GMP	51
4.3	Summary	52
	References	52
5	Salvage Pathways of Purine Nucleotide Biosynthesis	55
5.1	Introduction	55
5.2	Characteristics of Purine Salvage in Plants	56
5.3	Properties of Purine Phosphoribosyltransferases	59
5.3.1	Adenine Phosphoribosyltransferase	59
5.3.2	Hypoxanthine/Guanine Phosphoribosyltransferase	59
5.3.3	Xanthine Phosphoribosyltransferase	62
5.4	Properties of Nucleoside Kinases	62
5.4.1	Adenosine Kinase	62
5.4.2	Inosine/Guanosine Kinase	64
5.4.3	Deoxyribonucleoside Kinases	64

5.5	Properties of Nucleoside Phosphotransferase	65
5.6	Role of Purine Salvage in Plants	66
5.7	Summary	66
	References	66
6	Interconversion of Purine Nucleotides	71
6.1	Introduction	71
6.2	Deamination Reactions	71
6.2.1	Routes of Deamination of Adenine Ring	73
6.2.2	AMP Deaminase	73
6.2.3	Routes of Deamination of Guanine Ring	74
6.2.4	Guanosine Deaminase	75
6.3	Dephosphorylation Reactions	75
6.4	Glycosidic Bond Cleavage Reactions	76
6.4.1	Adenosine Nucleosidase	76
6.4.2	Inosine/Guanosine Nucleosidase	78
6.4.3	Non-specific Purine Nucleosidases	78
6.4.4	Recombinant Non-Specific Nucleosidases	78
6.5	<i>In Situ</i> Metabolism of ^{14}C -Labelled Purine Nucleotides	79
6.5.1	Metabolism of Adenine Nucleotides	79
6.5.2	Metabolism of Guanine Nucleotides	80
6.6	<i>In Situ</i> Metabolism of Purine Nucleosides and Bases	80
6.6.1	Metabolism of Adenine and Adenosine	82
6.6.2	Metabolism of Guanine and Guanosine	83
6.6.3	Metabolism of Hypoxanthine and Inosine	84
6.6.4	Metabolism of Xanthine and Xanthosine	84
6.6.5	Metabolism of Deoxyadenosine and Deoxyguanosine	85
6.7	Summary	88
	References	89
7	Degradation of Purine Nucleotides	95
7.1	Introduction	95
7.2	(S)-Allantoin Biosynthesis from Xanthine	97
7.2.1	Xanthine Dehydrogenase	99
7.2.2	Urate Oxidase	100
7.2.3	Allantoin Synthase	101
7.3	Catabolism of (S)-Allantoin	101
7.3.1	Allantoinase	103
7.3.2	Allantoate Amidohydrolase	104
7.3.3	(S)-Ureidoglycine Aminohydrolase	104
7.3.4	Allantoate Amidinohydrolase	105
7.3.5	Ureidoglycolate Amidohydrolase	105
7.3.6	(S)-Ureidoglycolate-urea Lyase	105
7.3.7	Urease	105
7.4	Purine Nucleotide Catabolism in Plants	106
7.5	Accumulation and Utilization of Ureides in Plants	107
7.5.1	Ureides in Plant Tissues and Xylem Sap	107

- 7.5.2 Role of Ureides in Nitrogen Storage and Transport 109
- 7.5.3 Role of Ureides in Germination and Development of Seeds 109
- 7.5.4 Ureide Formation in Nodules of Tropical Legumes 110
- 7.5.5 Other Role of Ureides in Plants 110
- 7.6 Summary 111
- References 111

Part III Pyrimidine Nucleotide Metabolism 117

- 8 Pyrimidine Nucleotide Biosynthesis *De Novo* 119
 - 8.1 Introduction 119
 - 8.2 Reactions and Enzymes of the *De Novo* Biosynthesis 121
 - 8.2.1 Synthesis of Carbamoyl-phosphate 121
 - 8.2.2 Formation of Carbamoyl-aspartate 123
 - 8.2.3 Formation of Dihydroorotase from Carbamoyl-aspartate 123
 - 8.2.4 Formation of Orotate from Dihydroorotate 124
 - 8.2.5 Synthesis of UMP from Orotate 125
 - 8.2.6 Synthesis of CTP from UTP 126
 - 8.3 Control Mechanism of *De Novo* Pyrimidine Ribonucleotide Biosynthesis 127
 - 8.3.1 Fine Control of the *De Novo* Pathway 127
 - 8.3.2 Coarse Control of the *De Novo* Pathway 129
 - 8.4 Biosynthesis of Thymidine Nucleotide 129
 - 8.4.1 Formation of dUMP 129
 - 8.4.2 Conversion of UMP to dUMP via dUTP 130
 - 8.4.3 Conversion of dUMP to dTMP 130
 - 8.4.4 Thymidine Monophosphate Kinase 131
 - 8.5 Summary 131
 - References 131
- 9 Salvage Pathways of Pyrimidine Nucleotide Biosynthesis 137
 - 9.1 Introduction 137
 - 9.2 Characteristics of Pyrimidine Salvage in Plants 137
 - 9.3 Enzymes of Pyrimidine Salvage 139
 - 9.3.1 Uracil Phosphoribosyl Transferase 140
 - 9.3.2 Uridine/Cytidine Kinase 142
 - 9.3.3 Thymidine Kinase 143
 - 9.3.4 Deoxyribonucleoside Kinase 144
 - 9.3.5 Nucleoside Phosphotransferase 144
 - 9.4 Role of Pyrimidine Salvage in Plants 145
 - 9.5 Summary 146
 - References 146

10	Interconversion of Pyrimidine Nucleotides	149
10.1	Introduction	149
10.2	Deaminase Reactions	149
10.2.1	Cytidine Deaminase	149
10.2.2	Cytosine Deaminase	152
10.2.3	Deoxycytidylate Deaminase	152
10.3	Nucleosidase and Phosphorylase Reactions	152
10.3.1	Uridine Nucleosidase	152
10.3.2	Thymidine Phosphorylase	153
10.4	<i>In Situ</i> Metabolism of ¹⁴ C-Labelled Pyrimidines	153
10.4.1	Metabolic Fate of Orotate	154
10.4.2	Metabolic Fate of Uridine and Uracil	154
10.4.3	Metabolic Fate of Cytidine and Cytosine	156
10.4.4	Metabolic Fate of Deoxycytidine	157
10.4.5	Metabolic Fate of Thymidine	158
10.5	Summary	159
	References	160
11	Degradation of Pyrimidine Nucleotides	165
11.1	Introduction	165
11.2	Enzymes Involved in the Degradation Routes of Pyrimidines	166
11.2.1	Dihydropyrimidine Dehydrogenase	167
11.2.2	Dihydropyrimidinase	167
11.2.3	β -Ureidopropionase	168
11.3	The Metabolic Fate of Uracil and Thymine	168
11.4	Summary	169
	References	170
Part IV Physiological Aspects of Nucleotide Metabolism 173		
12	Growth and Development	175
12.1	Introduction	175
12.2	Embryo Maturation	175
12.3	Germination	180
12.3.1	Purine Metabolism in Germination	180
12.3.2	Pyrimidine Metabolism in Germination	183
12.4	Organogenesis	185
12.5	Breaking Bud Dormancy	186
12.6	Fruit Ripening	186
12.7	Storage Organ Development and Sprouting	186
12.8	Suspension-Cultured Cells	187
12.8.1	Nucleotide Pools	187
12.8.2	Nucleotide Biosynthesis	188
12.8.3	Nucleotide Availability	188

12.9	Molecular Studies	189
12.10	Summary	189
	References	189
13	Environmental Factors and Nucleotide Metabolism	195
13.1	Introduction	195
13.2	Effect of Phosphate on Nucleotide Metabolism	195
13.3	Effect of Salts on Nucleotide Metabolism	199
13.4	Effect of Water Stress	202
13.5	Effect of Wound Stress	202
13.6	Effect of Iron Deficiency	205
13.7	Effect of Light	206
13.8	Summary	206
	References	206

Part V Purine Alkaloids 211

14	Occurrence of Purine Alkaloids	213
14.1	Introduction	213
14.2	Chemical Structure of Purine Alkaloids	213
14.3	Occurrence of Purine Alkaloids in Plants	215
14.3.1	Purine Alkaloids in Tea and Related Species	215
14.3.2	Purine Alkaloids in Coffee and Related Species	218
14.3.3	Purine Alkaloids in Maté	220
14.3.4	Purine Alkaloids in Cacao and Related Species	221
14.3.5	Purine Alkaloids in Cola Species	223
14.3.6	Purine Alkaloids in Guaraná and Related Species	223
14.3.7	Purine Alkaloids in Citrus Species	224
14.3.8	Purine Alkaloids in Other Plants	225
14.4	Summary	226
	References	226
15	Biosynthesis of Purine Alkaloids	231
15.1	Introduction	231
15.2	A Brief History of Caffeine Biosynthesis Research	231
15.3	Caffeine Biosynthesis Pathway	234
15.3.1	N-Methyltransferase Nomenclature	236
15.3.2	Formation of 7-Methylxanthine from Xanthosine	236
15.3.3	7-Methylxanthosine Synthase	237
15.3.4	N-Methylnucleosidase	240
15.3.5	Formation of Caffeine from 7-Methylxanthine	241
15.3.6	Caffeine Synthase	241
15.3.7	Theobromine Synthase	244
15.4	Genes and Proteins of Caffeine Synthase Family	245
15.5	Xanthosine Biosynthesis from Purine Nucleotides	249
15.5.1	De Novo Purine Route	250

15.5.2	Adenosine Monophosphate Route	251
15.5.3	S-Adenosyl-L-methionine Cycle Route	251
15.5.4	Nicotinamide Adenine Diphosphate Catabolism Route	252
15.5.5	Guanosine Monophosphate Route	253
15.6	Summary	253
	References	253
16	Physiological and Ecological Aspects of Purine Alkaloid Biosynthesis	259
16.1	Introduction	259
16.2	Physiology of Caffeine Biosynthesis	259
16.2.1	Purine Alkaloid Biosynthesis in Different Species	261
16.2.2	<i>Camellia</i>	261
16.2.3	<i>Coffea</i>	264
16.2.4	<i>Theobroma</i>	264
16.2.5	Maté	266
16.2.6	Guaraná	267
16.2.7	<i>Citrus</i>	268
16.3	Subcellular Localization of Caffeine Biosynthesis	268
16.3.1	Caffeine Synthase	268
16.3.2	The <i>De Novo</i> Route Enzymes	269
16.3.3	The AMP Route Enzymes	270
16.3.4	The SAM Route Enzymes	270
16.3.5	Subcellular Localization and Transport of Intermediates	270
16.4	Regulation of Caffeine Biosynthesis	270
16.5	Ecological Roles of Caffeine	271
16.5.1	Allelopathic Function Theory	271
16.5.2	Effect of Caffeine on Plant Growth	272
16.5.3	Allelopathy in Natural Ecosystems	273
16.5.4	Chemical Defence Theory	274
16.6	Summary	274
	References	275
17	Metabolism of Purine Alkaloids and Biotechnology	281
17.1	Introduction	281
17.2	Metabolism of Purine Alkaloids	281
17.2.1	Methylurate Biosynthesis	281
17.2.2	The Major Pathway of Caffeine Degradation	282
17.2.3	Purine Catabolic Pathways in Alkaloid Plants	284
17.3	Diversity of Purine Alkaloid Metabolism in Plants	285
17.3.1	<i>Coffea</i> Species	285
17.3.2	<i>Camellia</i> Species	286
17.3.3	Maté Species	290
17.3.4	Cacao Species	290
17.3.5	Other Plant Species	290
17.3.6	Bacteria	291
17.4	Biotechnology of Purine Alkaloids	293

- 17.4.1 Decaffeinated Coffee Plants 293
- 17.4.2 Decaffeinated Tea Plants 294
- 17.5 Caffeine-Producing Transgenic Plants 295
- 17.5.1 Antiherbivore Activity 295
- 17.5.2 Antipathogen Activity 296
- 17.6 Summary 298
- References 298

Part VI Pyridine Nucleotide Metabolism 301

- 18 Pyridine (Nicotinamide Adenine) Nucleotide Biosynthesis *De Novo* 303
 - 18.1 Introduction 303
 - 18.2 Two Distinct Pathways of *De Novo* Nicotinate Mononucleotide Biosynthesis 303
 - 18.3 The Outline of the *De Novo* Pathway of NAD Biosynthesis in Plants 304
 - 18.4 Enzymes Involved in *De Novo* NAD Synthesis in Plants 307
 - 18.4.1 L-Aspartate Oxidase and Quinolate Synthase 308
 - 18.4.2 Quinolate Phosphoribosyltransferase 309
 - 18.4.3 Nicotinate Mononucleotide Adenylyltransferase 309
 - 18.4.4 NAD Synthetase 310
 - 18.4.5 NAD Kinase 310
 - 18.5 Summary 310
 - References 310
- 19 Pyridine Nucleotide Cycle 315
 - 19.1 Introduction 315
 - 19.2 Pyridine Nucleotide Cycle 315
 - 19.2.1 Major Pyridine Nucleotide Cycles in Plants 317
 - 19.2.2 Alternative Pyridine Nucleotide Cycles in Plants 318
 - 19.2.3 Rate-Limiting Step of the Pyridine Cycle 319
 - 19.3 Catabolism of NAD 320
 - 19.3.1 Reactions from NAD to Nicotinate 320
 - 19.3.2 Degradation of Pyrimidine Ring 320
 - 19.3.3 Nicotinate Conversion to Nicotinate-*N*-Glucoside and *N*-Methylnicotinate 321
 - 19.4 Enzymes Involved in NAD Catabolism 321
 - 19.4.1 Direct NAD Cleavage Enzymes 321
 - 19.4.2 NAD Pyrophosphatase 321
 - 19.4.3 5'-Nucleotidase and Nicotinamide Riboside Nucleosidase 322
 - 19.4.4 Nicotinamidase and Nicotinamide Riboside Deaminase 322
 - 19.5 Salvage of Nicotinamide and Nicotinate 323
 - 19.5.1 Nicotinate Phosphoribosyltransferase 323
 - 19.5.2 Nicotinate Riboside Kinase 324
 - 19.6 Summary 325
 - References 325

Part VII Pyridine Alkaloids 329

- 20 Occurrence and Biosynthesis of Pyridine Alkaloids 331
- 20.1 Introduction 331
- 20.2 Occurrence of Pyridine Alkaloids 333
- 20.2.1 Trigonelline in Plants 333
- 20.2.2 Other Pyridine Alkaloids in Plants 334
- 20.3 Biosynthesis of Pyridine Alkaloids 335
- 20.3.1 Trigonelline Biosynthesis 335
- 20.3.2 Nicotinate *N*-Glucoside Biosynthesis 336
- 20.3.3 The Diversity of Biosynthetic Reactions 337
- 20.3.3.1 Ferns 338
- 20.3.3.2 Gymnosperms 338
- 20.3.3.3 Angiosperms 339
- 20.3.3.4 Nicotinate Conjugate Formation 340
- 20.3.4 Biosynthesis of Ricinine 341
- 20.3.5 Biosynthesis of Nicotine (Pyridine Ring) 343
- 20.4 Summary 345
- References 345
- 21 Physiological Aspect and Biotechnology of Trigonelline 351
- 21.1 Introduction 351
- 21.2 Physiological Aspect of Trigonelline Biosynthesis 351
- 21.2.1 Coffee 351
- 21.2.2 Leguminous Plants 354
- 21.3 Physiological Aspects of Nicotinate *N*-Glucoside Biosynthesis 356
- 21.4 The Role of Trigonelline in Plants 356
- 21.4.1 Role of Trigonelline as a Nutrient Source 357
- 21.4.2 Role of Trigonelline as a Compatible Solute 357
- 21.4.3 Trigonelline and Nyctinasty 358
- 21.4.4 Cell Cycle Regulation 358
- 21.4.5 Detoxification of Nicotinate 359
- 21.4.6 Signal Transduction 360
- 21.4.7 Role of Host Selection by Herbivores 360
- 21.5 Biotechnology of Trigonelline 360
- 21.6 Summary 362
- References 363

Part VIII Other Nucleotide-Related Metabolites 367

- 22 Sugar Nucleotides 369
- 22.1 Introduction 369
- 22.2 The Sugar Nucleotide Moiety 370
- 22.3 Enzymes of Sugar Nucleotide Biosynthesis 371
- 22.3.1 UDP-Glucose Pyrophosphorylase 371
- 22.3.2 UDP-Sugar Pyrophosphorylase 374

22.3.3	Sucrose Synthase	376
22.4	Localization of UDP-Glucose-Producing Enzymes	377
22.5	UDP-Glucose-Interconversion	377
22.6	Other Metabolites	379
22.6.1	Cyclic Nucleotides	379
22.6.2	Diadenosine Tetrphosphate	381
22.6.3	Purine Alkaloid Glucosides	382
22.7	Summary	382
	References	382
23	Cytokinins	387
23.1	Introduction	387
23.2	Adenosine Phosphate-Isopentenyl Formation	388
23.3	<i>trans</i> -Zeatin Phosphate Synthesis	389
23.4	Formation of Cytokinin Bases	389
23.5	Effect of Nucleotide Enzymes in Cytokinins	390
23.5.1	Cytokinin Inactivation by Adenine Phosphoribosyltransferase	390
23.5.2	Homeostasis of Cytokinin by Adenosine Kinase	392
23.5.3	Endodormancy of Potato and Purine Nucleoside Phosphorylase	392
23.6	New Purine-Related Plant Growth Regulators	392
23.7	Summary	393
	References	394

Part IX Dietary Plant Alkaloids, Their Bioavailability, and Potential Impact on Human Health 397

24	Bioavailability and Potential Impact on Human Health of Caffeine, Theobromine, and Trigonelline	399
24.1	Caffeine	399
24.1.1	Dietary Caffeine	399
24.1.2	Bioavailability and Bioactivity of Caffeine	400
24.2	Theobromine	404
24.2.1	Interactions with Flavan-3-ols	404
24.2.2	Toxicity of Theobromine	406
24.3	Trigonelline	406
24.3.1	Dietary Trigonelline	406
24.3.2	Bioavailability and Bioactivity of Trigonelline	407
24.4	Summary	409
	References	409