

Contents

1	Advances in Biocompatibility: A Prerequisite for Biomedical Application of Biopolymers	1
	<i>Matthew R. Jorgensen, Helin Räägel, and Thor S. Rollins</i>	
1.1	Introduction	1
1.2	Biocompatibility Evaluation of Biopolymeric Materials and Devices	2
1.3	Using a Risk-Based Approach to Biocompatibility	4
1.3.1	Chemistry of Biopolymers and Risk	6
1.3.2	Chemistry Screening of Biopolymers	7
1.4	Specific Biological Endpoint Evaluations	11
1.4.1	Cytotoxicity	11
1.4.2	Systemic Toxicity (Acute, Subacute, Subchronic, and Chronic)	12
1.4.3	Implantation	14
1.5	Conclusion	15
	References	16
2	Advanced Microbial Polysaccharides	19
	<i>Filomena Freitas, Cristiana A.V. Torres, Diana Araújo, Inês Farinha, João R. Pereira, Patrícia Concórdio-Reis, and Maria A.M. Reis</i>	
2.1	Introduction	19
2.2	Functional Properties and Applications of Microbial Polysaccharides	20
2.3	Commercially Relevant Microbial Polysaccharides: Established Uses and Novel/Prospective Applications	22
2.3.1	Pullulan	22
2.3.2	Scleroglucan	23
2.3.3	Xanthan Gum	23
2.3.4	Dextrans	24
2.3.5	Curdlan	24
2.3.6	Gellan Gum	24
2.3.7	Levan	25
2.3.8	Hyaluronic Acid	25
2.4	Hydrogels Based on Microbial Polysaccharides	25
2.5	Bionanocomposites Based on Microbial Polysaccharides	29

2.6	Bioactive Polysaccharides from Microalgae: An Emerging Area	32
2.6.1	Polysaccharide-Producing Microalgae	33
2.6.2	Biological Activity and Potential Applications	33
2.6.2.1	Antiviral Activity	36
2.6.2.2	Immunomodulatory, Anti-inflammatory, and Anticancer Activities	36
2.6.2.3	Anticoagulant and Antithrombotic Activity	38
2.6.2.4	Antioxidant Activity	38
2.6.2.5	Other Biological Properties	39
2.6.3	Commercialization Prospects	39
2.7	Applications of Chitinous Polymers	40
2.7.1	Chitin, Chitosan, and Chitinous Polysaccharides	40
2.7.2	Properties of Chitinous Polysaccharides	41
2.7.3	Applications of Chitinous Polysaccharides	41
2.7.3.1	Biomedical Applications	42
2.7.3.2	Pharmaceutical Applications	43
2.7.3.3	Food Applications	43
2.7.3.4	Other Applications	43
2.8	Microbial Polysaccharides: A World of Opportunities	44
	Acknowledgments	45
	References	45
3	Microbial Cell Factories for Biomanufacturing of Polysaccharides	63
	<i>M. Fata Moradali and Bernd H.A. Rehm</i>	
3.1	Introduction	63
3.2	Prominent Microbial Polysaccharides and Their Properties and Applications	63
3.2.1	Xanthan and Acetan	64
3.2.2	Succinoglycan and Galactoglucan	64
3.2.3	Sphingan Polysaccharides	66
3.2.4	Pullulan	66
3.2.5	Cellulose and Curdlan	67
3.2.6	Alginates	67
3.2.7	Hyaluronic Acid or Hyaluronate	68
3.2.8	Dextrans	68
3.2.9	Levan and Inulin	69
3.3	Biosynthesis Pathways of Bacterial Polysaccharides	69
3.3.1	Genetic Background Required for Biosynthesis of Polysaccharides in Bacteria	70
3.3.2	Production of Active Precursor, Polymerization, and Polysaccharide Modifications	71
3.3.3	Regulatory Pathways and Posttranslational Modifications	72
3.4	Strategies for Engineering Cell Factories	76
3.4.1	Enhancement of Productivity upon the Energetic State of the Cell and Metabolites	77
3.4.2	Genetic and Metabolic Engineering of Cell Factories	78

3.4.3	Strategies for Optimizing Physicochemical Properties of Polysaccharides	79
3.4.4	Recombinant Production of Polysaccharides and Tailor-Made Products	83
3.5	Conclusion and Future Perspective	86
	Acknowledgments	87
	References	87
4	Exploitation of Exopolysaccharides from Lactic Acid Bacteria	103
	<i>Tsuda Harutoshi</i>	
4.1	Introduction	103
4.1.1	Lactic Acid Bacteria	103
4.1.2	Exopolysaccharides	103
4.1.3	Importance of PS Produced by LAB	105
4.2	Homo-PS	105
4.2.1	Biosynthesis	105
4.2.2	Composition and Structure	106
4.2.3	Instability of Homo-PS Production	106
4.3	Hetero-PS	111
4.3.1	Biosynthesis	111
4.3.2	Monosaccharides Composition of Hetero-PS	111
4.3.3	Yield of Hetero-PS	112
4.3.4	Instability of Hetero-PS Production	116
4.4	Prebiotic Activity	117
4.4.1	Commercial Prebiotic Oligosaccharides	117
4.4.2	Prebiotic Polysaccharides	118
4.4.3	Prebiotics in Japanese FOSHU	119
4.4.4	Prebiotics Produced by LAB	119
4.5	Conclusion	120
	References	120
5	Nanocellulose: A New Biopolymer for Biomedical Application	129
	<i>Hippolyte Durand, Megan Smyth, and Julien Bras</i>	
5.1	Trends of Biobased Polymers in Biomedical Application	129
5.1.1	Introduction to Biomedical Engineering	130
5.1.2	Overview of Biobased Materials for Biomedical Applications	132
5.1.2.1	Biomaterials: A Definition	132
5.1.2.2	Biobased Polymers	135
5.1.2.3	Cellulose as a Biomaterial	138
5.2	Nanocellulose: Production, Characterization, Application, and Commercial Aspects	142
5.2.1	Isolation and Characterization of Nanocellulose Materials	143
5.2.1.1	Cellulose Nanocrystals	144
5.2.1.2	Cellulose Nanofibrils	145

- 5.2.1.3 Bacterial Nanocellulose (BNC) 149
- 5.2.2 Characterization of Cellulosic Nanomaterials (CNMs) 151
- 5.2.3 Industrialization of Nanocellulose: First and Upcoming Applications 153
- 5.2.4 Health and Toxicology: A Concern for CNM Development in Biomedical Field 154
- 5.2.5 Cellulose Nanofibrils and Medical Applications 164
- 5.3 Conclusions and Perspectives 170
- References 170

- 6 Advances in Mucin Biopolymer Research: Purification, Characterization, and Applications 181**
Matthias Marczynski, Benjamin Winkeljann, and Oliver Lieleg
- 6.1 Introduction 181
- 6.2 Mucin Sources and Purification Process 182
- 6.3 Structure–Function Relation of Mucins 185
- 6.4 Characterizing Mucins and Mucin-Based Materials 187
- 6.5 Biomedical Applications of Purified Mucins 190
- 6.5.1 Eye Drops or Contact Lens Coatings 190
- 6.5.2 Mouth Sprays 192
- 6.5.3 Artificial Joint Fluids 192
- 6.5.4 Coatings of Medical Devices 193
- 6.5.5 Components of Hydrogels for Drug Delivery 194
- 6.5.6 Molecular Standards for Lab Tests with Clinical Mucus Samples 194
- 6.6 Outlook: Engineered Mucins and Mucin-Mimetic Polymers 194
- Acknowledgments 195
- References 195

- 7 Advances in the Synthesis of Fibrous Proteins and Their Applications 209**
Gang Wei, Xi Ma, Yaru Bai, Coucong Gong, and Yantu Zhang
- 7.1 Introduction 209
- 7.2 Synthesis, Structure, and Characterizations of Fibrous Protein Materials 210
- 7.2.1 Synthesis Methods 210
- 7.2.2 Structure 212
- 7.2.3 Characterizations 213
- 7.3 Applications of Fibrous Protein Materials 213
- 7.3.1 Bone Tissue Engineering 213
- 7.3.2 Biomedical Engineering 215
- 7.3.3 Sensors and Biosensors 216
- 7.3.4 Nanodevices 217
- 7.3.5 Energy Application 218
- 7.3.6 Environmental Application 220
- 7.4 Conclusions 223
- Acknowledgments 224
- References 224

8	Microbial Polyhydroxyalkanoates (PHAs): From Synthetic Biology to Industrialization	231
	<i>Yuki Miyahara, Ayaka Hiroe, Shunsuke Sato, Takeharu Tsuge, and Seiichi Taguchi</i>	
8.1	Introduction	231
8.2	Synthetic Biology for Production of Kaneka PHBH	233
8.2.1	Isolation of Bacterium Producing Poly(3-hydroxybutyrate-co-3-hydroxyhexanoate)	233
8.2.2	Material Properties of PHBH	234
8.2.3	Industrial PHBH Production Process	235
8.2.4	Molecular Breeding of PHBH-Producing Bacteria	236
8.2.5	Precise Control of 3HHx Fraction by Genetic Modification of <i>Ralstonia eutropha</i>	238
8.2.6	Business Plan for Kaneka PHBH Industrialization	239
8.3	Synthetic Biology for Production of Medium-Chain-Length PHAs with Homogeneous Side-Chain Lengths (Homo-PHAs)	240
8.3.1	Copolymers Based on Medium-Chain-Length PHA Monomeric Constituents	240
8.3.2	Pathway Engineering for Homo-PHA Production	242
8.3.3	Improved Microbial Production of Homo-PHAs	243
8.3.4	Material Properties of Homo-PHAs	245
8.3.5	Integrated Production Process of Homo-PHAs from Renewable Feedstock	246
8.4	Synthetic Biology for Production of Lactate-Based Polymers	247
8.4.1	Creation of Lactate-Polymerizing Enzyme (LPE)	247
8.4.2	Biosynthesis of Lactate-Based Polymers	249
8.4.3	Integrated Production Process of Lactate-Based Polymers from Renewable Feedstock	251
8.4.4	Biosynthesized Lactate-Based Polymer Shows Superior Properties	253
8.5	Outlook	254
	References	255
9	Natural and Synthetic Biopolymers in Drug Delivery and Tissue Engineering	265
	<i>John D. Schneible, Michael A. Daniele, and Stefano Menegatti</i>	
9.1	Introduction	265
9.2	Synthetic and Natural Substrates	267
9.3	Applications of Natural and Synthetic Polypeptides	267
9.3.1	Drug Delivery Vehicles	267
9.3.2	Targeting Agents	273
9.3.3	Cell-Permeating Peptides	274
9.3.4	Peptides in Tissue Engineering and Regenerative Medicine	276
9.4	Applications of Polysaccharides	280
9.4.1	Drug Delivery	280
9.4.2	Tissue Engineering and Regenerative Medicine	284
9.5	Conclusions and Future Outlook	290
	References	290

10	Biopolymers in Regenerative Medicine: Overview, Current Advances, and Future Trends	357
	<i>Michael R. Behrens and Warren C. Ruder</i>	
10.1	Introduction	357
10.2	Biopolymer Scaffold Assembly	358
10.2.1	Hydrogel Biopolymer Scaffolds	358
10.2.2	Electrospinning of Biopolymer Scaffolds	360
10.2.3	Three-Dimensional Printing of Biopolymer Scaffolds	362
10.3	Organ System Specific Biopolymer Scaffolds	367
10.3.1	Biopolymers for Musculoskeletal System Regeneration	368
10.3.1.1	Biopolymers for Bone Regeneration	368
10.3.1.2	Biopolymers for Cartilage Regeneration	370
10.3.1.3	Biopolymers for Ligament and Tendon Regeneration	371
10.3.2	Biopolymers for Cardiovascular System Regeneration	372
10.3.2.1	Biopolymers for Vascular Regeneration	373
10.3.2.2	Biopolymers for Cardiac Regeneration	374
10.4	Summary and Outlook	376
	References	377
	Index	381