## **Contents**

## Preface xi

1	Introduction to Freeze-drying and Ice Templating $\ 1$
1.1	Introduction 1
1.2	The Freeze-drying Process 3
1.2.1	Additives in the Solution 4
1.2.1.1	Additives to Maintain Integrity/Activity of Biological Samples
1.2.1.2	Lyoprotectants to Prevent Denaturation of Biopharmaceutics of
	Enhance Reconstitution of Pharmaceutics 5
1.2.1.3	Stabilizer/Binders for Particulate Suspensions 5
1.2.2	Optimizing the Freezing Stage 5
1.2.3	Primary Drying in Freeze-drying 7
1.2.4	Secondary Drying in Freeze-drying 9
1.3	Ice Templating for Porous Structures 10
1.3.1	Solutes or Particles 10
1.3.2	Solvents 11
1.3.3	Controlled Freezing 12
1.3.3.1	Control Orientation of Ice Crystal Growth 12
1.3.3.2	Ways of Freezing Samples 13
1.3.4	Removal of Ice Crystal Templates 14
1.3.5	Ice-templated Materials 15
1.3.5.1	Shape and Form 15
1.3.5.2	Pore Structure and Morphology 16
1.3.5.3	Type of Materials 18
1.4	The Practice in Our Laboratory 18
1.4.1	Controlled Freezing 18
1.4.2	Observation of Freezing and Freeze-drying 20
1.4.3	Freeze-drying Procedure 22
	References 24
2	Fundamentals of Controlled Freezing for Ice-templated Porous
	Materials 29
2.1	Introduction 29

The Basics of Ice Crystals 30



2.2

vi	Contents
----	----------

3.5.1.2	During Freeze-drying 77
3.5.1.3	During Solid State Storage 78
3.5.2	Biopharmaceutical Formulations 81
3.5.2.1	Peptide Formulations 82
3.5.2.2	Protein Formulations 83
3.5.2.3	Vaccine Formulations 85
3.5.2.4	Nucleic Acid-based Formulations 87
3.6	Freeze-drying in Food Applications 89
3.6.1	Simple Freeze-drying 89
3.6.2	Encapsulation 90
3.6.3	Probiotic Foods 90
3.7	Summary 92
	References 92
4	Porous Polymers by Ice Templating 103
4.1	Introduction 103
4.2	Porous Polymers by Freeze-drying of Solutions and Suspensions 104
4.2.1	Polymer Sponges 104
4.2.2	Aligned Porous Polymers by Directional Freezing 106
4.2.2.1	Water-based Systems 107
4.2.2.2	Organic Solvent-based Systems 108
4.2.2.3	Compressed CO <sub>2</sub> Solution 110
4.2.3	Nanofibrous Polymers 111
4.2.4	Combining Ice Templating and Other Templating Methods 112
4.3	Hydrogels and Crosslinked Porous Polymers 114
4.3.1	Hydrogels By a Freeze–thaw Process 114
4.3.2	Macroporous Cryogels 116
4.3.3	Aligned Porous Materials By Frozen Polymerization 118
4.3.4	Post-freeze-drying Crosslinking 120
4.4	Applications 121
4.4.1	Biocompatibility and Tissue Engineering 121
4.4.2	Controlled Drug Release 124
4.4.3	Encapsulation 125
4.4.4	Water Treatment 127
4.4.5	Liquid Chromatography and Separation 129
4.4.6	Other Applications 130
4.5	Summary 130
	References 131
_	Danis Carrania and Madala harlas Tanas India a 141
5	Porous Ceramics and Metals by Ice Templating 141
5.1	Introduction 141  Paraus Coronics by Joe Tompleting 142
5.2	Porous Ceramics by Ice Templating 142  Effect of Formulations 142
5.2.1	Effect of Formulations 142 Ceramic Particles 142
5.2.1.1	
5.2.1.2	331.311
5.2.1.3 5.2.1.4	Dispersant or Stabilizer 146 Binder 147
J.Z.I.4	DINUCI 17/

5.2.1.5 5.2.2 5.2.2.1 5.2.2.2 5.3 5.3.1 5.3.2 5.3.3 5.4 5.5 5.6 5.6.1 5.6.2 5.6.3 5.6.4 5.6.5 5.7	Additives 147 Freezing Conditions 150 Modes of Processing and Freezing 150 Freezing Velocities 157 Porous Ceramics by Gelation-Freeze-Casting 158 Gelation with Gelatin 158 Photopolymerization (or Photocuring) of Frozen Slurry 158 Polymerization (or Gelation) of Slurry 159 Porous Ceramics via Cryo-Sol-Gelation 159 Porous Metals via Ice templating 162 Applications of Ice-templated Ceramics 163 Filtration/Gas Permeation 163 Thermal Insulator 163 Bioceramics 165 Electric/electrode Materials 166 Catalysis 167 Summary 168 References 169
6	Strong and Tough Ceramic Composites via Ice
	Templating 177
6.1	Introduction 177
6.1.1	Enhanced Applications by Ceramic Composites 177
6.1.2	Processing and Mechanical Behaviour of Ceramic Composites 179
6.2	Mechanical Characterizations of Ceramic Composites 182
6.2.1	Strength 182
6.2.2	Hardness 185
6.2.3	Fracture Mechanics and Fracture Toughness 186
6.2.4	Toughening Mechanism in Ceramics and Ceramic Composites 187
6.3	Porous Ceramic/Polymer Composites 189
6.3.1	Hydroxyapatite (HA)-based Composites 191
6.3.2	Clay-based Composites 193
6.4	Porous Ceramic–Ceramic Composites 196
6.5	Nacre-like Layered Ceramic–Polymer Composites 198
6.5.1	Nacre and Nacre-mimic Composites 198
6.5.2	Layered Polymer-Ceramic Composites by Infiltrating Ice-templated
	Porous Ceramics 200
6.5.3	Magnetic Field-assisted Freeze-casting for Strong Composites 207
6.6	Nacre-like Ceramic/Metal Composites 209
6.7	Enamel-mimic Ceramic–Polymer Composites 211
6.8	Ceramic-Ceramic Composites with the Second Nanoscale
	Ceramic Phase 214
6.9	Tough and Functional Composites 216
6.10	Summary 218
	References 219

7	Porous Carbon and Carbon-based Materials via Ice Templating
	and Freeze-drying 229
7.1	Introduction 229
7.2	Carbon Cryogels and Ice-templated Carbons 230
7.2.1	Carbon Cryogels 230
7.2.2	Ice-templated Carbons 237
7.3	Carbon Nanofibres 241
7.4	Carbon Nanotubes (CNTs) and CNT-based Materials 245
7.4.1	Introduction to CNTs 245
7.4.2	CNT Aerogels/Cryogels 246
7.4.3	CNT-based Porous Materials 247
7.5	Porous Graphene Networks and Graphene-based Materials 250
7.5.1	Graphene and 3D Graphene Networks 250
7.5.2	Porous Graphene by Ice Templating/Freeze-drying 251
7.5.3	Graphene-based or Graphene-containing Materials by Ice
	Templating 258
7.6	Porous Graphene/CNT Hybrid Structures 261
7.7	Summary 264
	References 265
8	Nanomedicine via Freeze-drying and Ice Templating 277
8.1	Introduction 277
8.2	Poorly Water-soluble Drugs and Drug Classifications 277
8.3	Nanoformulation Approaches for Poorly Soluble Drugs 280
8.4	Bioavailability and Delivery of Drug Nanoparticles 284
8.4.1	The Absorption Process 284
8.4.1.1	The Orally Administering Route 285
8.4.1.2	Absorption in Lung by Pulmonary Delivery 288
8.4.2	Nanoparticle Clearance and Distribution 289
8.4.3	Metabolism and Excretion 291
8.4.4	Nanoparticle Toxicology 293
8.5	Freeze-drying of Solutions/Suspensions for Nanomedicine 294
8.6	Emulsion-Freeze-drying for Drug Nanoparticles 295
8.7	Solvent Evaporation Within Porous-Soluble Polymers 301
8.8	Summary 303
	References 304
9	Nanostructured Materials Fabricated via Ice Templating of
	Colloidal/Nanoparticle Suspensions 313
9.1	Introduction 313
9.2	Cellulose Nanofibres (CNFs) and Cellulose Nanocrystals (CNCs) 314
9.3	Nanoparticles and Colloids 318
9.4	Nanowires and Nanofibres 323
9.5	Platelets and Nanosheets 323
9.6	Mixing Colloids and Core–Shell Nanoparticles 325
9.7	Summary 327
	References 328

X	Contents
---	----------

10	Other Developments and Perspectives in the Fabrication of New Materials Facilitated by Freezing and Freeze-drying 333
10.1	Combining Ice-templating and Other Techniques 333
10.1.1	Ice Templating and Emulsion Templating 333
10.1.2	Gelation/Crosslinking and Ice Templating 335
10.1.3	Ice Templating with Green Solvents 336
10.2	Freezing-induced Self-assembly 337
10.3	Reaction and Polymerization in Frozen Solutions 337
10.4	Ice-templated Hierarchically Porous Materials Containing
	Micropores 341
10.5	General Summary and Perspectives 344
	References 345

Index 349