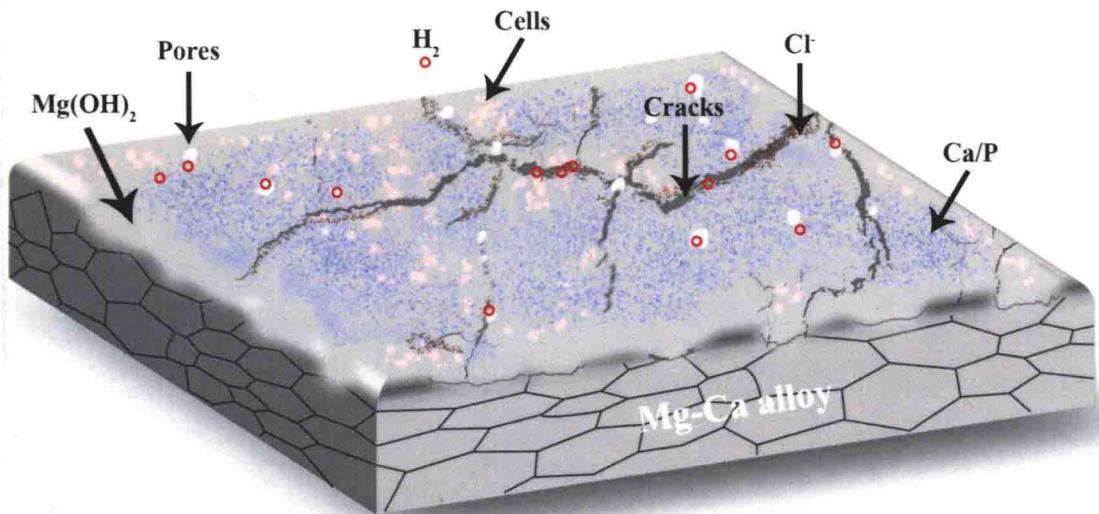


Magnesium Alloys as Degradable Biomaterials



Yufeng Zheng

Magnesium Alloys as Degradable Biomaterials

Yufeng Zheng



CRC Press

Taylor & Francis Group

Boca Raton London New York

CRC Press is an imprint of the
Taylor & Francis Group, an **Informa** business

CRC Press
Taylor & Francis Group
6000 Broken Sound Parkway NW, Suite 300
Boca Raton, FL 33487-2742

© 2016 by Taylor & Francis Group, LLC
CRC Press is an imprint of Taylor & Francis Group, an Informa business

No claim to original U.S. Government works

Printed on acid-free paper
Version Date: 20150727

International Standard Book Number-13: 978-1-4665-9804-1 (Hardback)

This book contains information obtained from authentic and highly regarded sources. Reasonable efforts have been made to publish reliable data and information, but the author and publisher cannot assume responsibility for the validity of all materials or the consequences of their use. The authors and publishers have attempted to trace the copyright holders of all material reproduced in this publication and apologize to copyright holders if permission to publish in this form has not been obtained. If any copyright material has not been acknowledged please write and let us know so we may rectify in any future reprint.

Except as permitted under U.S. Copyright Law, no part of this book may be reprinted, reproduced, transmitted, or utilized in any form by any electronic, mechanical, or other means, now known or hereafter invented, including photocopying, microfilming, and recording, or in any information storage or retrieval system, without written permission from the publishers.

For permission to photocopy or use material electronically from this work, please access www.copyright.com (<http://www.copyright.com/>) or contact the Copyright Clearance Center, Inc. (CCC), 222 Rosewood Drive, Danvers, MA 01923, 978-750-8400. CCC is a not-for-profit organization that provides licenses and registration for a variety of users. For organizations that have been granted a photocopy license by the CCC, a separate system of payment has been arranged.

Trademark Notice: Product or corporate names may be trademarks or registered trademarks, and are used only for identification and explanation without intent to infringe.

Visit the Taylor & Francis Web site at
<http://www.taylorandfrancis.com>

and the CRC Press Web site at
<http://www.crcpress.com>



Printed and bound in Great Britain by
TJ International Ltd, Padstow, Cornwall

Magnesium Alloys as Degradable Biomaterials

Preface

Biodegradable metals (BMs) are metals expected to corrode gradually *in vivo*, with an appropriate host response elicited by released corrosion products, then dissolve completely upon fulfilling the mission to assist with tissue healing with no implant residues (Zheng 2013). As the main force of the BM family, Mg and its alloys have been widely studied as potential biomaterials and have attracted the attention of biomaterial scientists and medical device societies. Up to the present, a full chain from material selection and properties optimization of Mg alloys, processing into semiproducts and surface treatment, device design, and manufacturing of the final devices to animal testing and clinical trials of the final Mg alloy implants have been conducted. Various medical device prototypes have been designed, including cardiovascular stents, bone staples, ACL screws, nonvascular stents, and clips, and some of them have been clinically trialed in Europe, China, and South Korea. One kind of Mg alloy device is now available on the European market as an implant for commercial sales. Every year since 2009, an international symposium on biodegradable metals for biomedical applications (<http://www.biodegradablenet.org/>) has been held, and, moreover, scientific journals and patent databases have recorded a high increase in publications in this area.

The research on biodegradable Mg alloys designed as degradable metallic biomaterials has been mature, and this book aims to provide a comprehensive description of magnesium and its alloys designed as biodegradable metallic implant materials. The basic concepts of biodegradation mechanisms of Mg and its alloys, the strategy to control their biodegradation mode and rate, microstructure, mechanical property, corrosion resistance to body fluids, and *in vitro* and *in vivo* biocompatibility are introduced. Then various types of new biomedical Mg alloy systems will be enumerated with their special properties illustrated. Finally, the medical devices of biomedical Mg alloys will be designed and analyzed with numerical calculation and animal trials. The book provides a wealth of updated research information for graduate students, teachers, and research workers in the fields of materials science, biomedical engineering, and clinical medicine and dentistry and also for professionals involved in implantable medical device design and manufacturing.

I would like to thank colleagues working in the field of biodegradable metals all over the world and especially the majority of the attendants at the international symposiums on biodegradable metals from 2009 to the present. As a co-chair with Prof. Diego Mantovani, Prof. Frank Witte, and Prof. Mark Staiger, I get together with 120–150 scholars during the last week of August every year, sharing the research progress on biomedical Mg alloys with topics on new material fabrication, biodegradation, *in vitro* and *in vivo* testing, device design, and clinical trials, with a panel discussion on proposing international standardization on the materials and device evaluations. I get a lot of inspiration through listening and discussing with scholars from all over the world during the conferences.

Special thanks must be given to my students at the Laboratory of Biomedical Materials and Devices, Department of Materials Science and Engineering, College

of Engineering, Peking University (<http://lbmd.coe.pku.edu.cn/>) for helping me on the manuscript preparation, typing, and copyright licensing transaction. They are Yang Liu (Chapters 1, 4, and 9), Nan Li (Chapters 2, 12, and 14), Dong Bian (Chapters 5, 10, and 11), Yuanhao Wu (Chapters 6, 7, and 8), Zhen Zhen (Chapter 3), Xiaochen Zhou (Chapter 13), Meng Zhou (Chapter 2), and Weirui Zhou (Chapters 5 and 10). I am very grateful to the funding bodies including the National Basic Research Program of China (973 Program; Grant No. 2012CB619102), the National Science Fund for Distinguished Young Scholars (Grant No. 51225101), the National Natural Science Foundation of China (Grant No. 51431002 and 31170909), the NSFC/RGC Joint Research Scheme under Grant No. 51361165101, the Beijing Municipal Science and Technology Project (Z131100005213002), and the State Key Laboratory for Mechanical Behavior of Materials (Grant No. 20141615).

Author

Dr. Yufeng Zheng earned his PhD in materials science from the Harbin Institute of Technology, China, in 1998. From 1998 to 2004, he was assistant professor (1998–2000), associate professor (2000–2003), and full professor (2003–2004) at the Harbin Institute of Technology, China, and since 2004, he has been a full professor at Peking University in Beijing, China.

Dr. Zheng has authored or co-authored more than 300 scientific peer-reviewed articles, has been cited more than 5800 times, and has an H-index of 37. He served as a member of the editorial board of the *Journal of Biomedical Materials Research-Part B: Applied Biomaterials* (Wiley), *Journal of Biomaterials and Tissue Engineering* (American Scientific Publishers), *Materials Letters* (Elsevier), *Intermetallics* (Elsevier), *Journal of Materials Science & Technology* (Elsevier), *Frontiers of Materials Science* (Springer), *Acta Metallurgica Sinica (English Letters)* (Springer), and *Journal of Orthopaedic Translation* (Elsevier). His areas of special interest include the development of various new biomedical metallic materials (beta-Ti alloys with low elastic modulus, biodegradable Mg alloys and Fe alloys, bulk metallic glass, bulk nanocrystalline materials, etc.). Dr. Zheng has received several awards, including New Century Excellent Talents in University awarded by the Ministry of Education of China (2007) and Distinguished Young Scholars awarded by the Natural Science Foundation of China (2012).

Contents

Preface.....	xix
Author	xxi
Chapter 1 Introduction	1
1.1 Property and Function of Element Mg	1
1.2 History of Mg and Its Alloys for Biomedical Applications	2
1.2.1 Before 2000.....	2
1.2.2 After 2000	2
1.3 Design of Mg and Its Alloys for Biomedical Applications	6
1.3.1 Selection of Alloying Elements to Mg for Better Performance	6
1.3.1.1 Calcium.....	6
1.3.1.2 Zinc	8
1.3.1.3 Strontium	8
1.3.1.4 Silver	8
1.3.1.5 Lithium	8
1.3.1.6 Rare Earth Elements.....	9
1.4 Comparison with Other Biomaterials.....	9
1.4.1 Comparison with Bioinert Metallic Materials	9
1.4.2 Comparison with Biodegradable Ceramics and Polymers	11
1.4.2.1 Biodegradable Ceramics.....	11
1.4.2.2 Biodegradable Polymers	11
1.4.2.3 Comparison.....	11
1.4.3 Comparison with Other Biodegradable Metals.....	13
1.4.3.1 General Introduction to Biodegradable Metals	13
1.4.3.2 Degradation Mechanism.....	15
1.5 General Analytical Methods for Biodegradable Mg and Its Alloys	16
1.5.1 Chemical and Microstructural Characterization	17
1.5.1.1 Metallographic Observation and Scanning Electron Microscope (SEM) Observation	17
1.5.1.2 X-Ray Diffraction (XRD) Characterization	17
1.5.2 Mechanical Property	17
1.5.2.1 Tension	18
1.5.2.2 Three-Point Bending	18
1.5.2.3 Wear.....	18
1.5.2.4 Fatigue	19

1.5.3	Biodegradation Behavior and Ion Release	20
1.5.3.1	Corrosion Medium Selection	20
1.5.3.2	Electrochemical Measurement	20
1.5.3.3	Immersion Test	24
1.5.3.4	Hydrogen Evolution Test.....	25
1.5.4	Cytotoxicity (Extract Preparation)	25
1.5.4.1	Extract Preparation	26
1.5.4.2	Extract Concentration.....	28
1.5.4.3	Cell Lines or Primary Cells.....	28
1.5.4.4	Protein Effect.....	29
1.5.5	Hemocompatibility	29
1.5.6	Animal Testing	30
1.5.6.1	Bone Repair	30
1.5.6.2	Stent Application	32
Chapter 2	Biodegradation Mechanism and Influencing Factors of Mg and Its Alloys.....	37
2.1	Biodegradation Mechanism of Pure Mg in the Physiological Environment.....	37
2.2	Influence of Alloying Elements and Impurities on the Biodegradation of Mg and Its Alloys	40
2.3	Degradation Mode and Rate of Mg and Its Alloys in the Physiological Environment.....	42
2.3.1	Modes of Corrosion.....	42
2.3.1.1	Galvanic Corrosion	42
2.3.1.2	Localized Corrosion	42
2.3.1.3	Fretting Corrosion.....	44
2.3.1.4	Stress Corrosion Cracking	44
2.3.1.5	Corrosion Fatigue	45
2.3.2	In Vitro and In Vivo Degradation Rate	46
2.4	Influence of Environmental Variables on the Biodegradation of Mg and Its Alloys	49
2.4.1	Temperature.....	50
2.4.2	Chemical Composition of Corrosion Media	50
2.4.2.1	Inorganic Ions	50
2.4.2.2	Buffer	52
2.4.2.3	Amino Acid and Proteins	52
2.4.3	Solution Volume and Flow	53
2.5	Biological Effects of Degradation Products	55
2.5.1	Biological Effects of Mg and Its Alloying Elements ...	56
2.5.2	Biological Effect of Hydrogen.....	62
2.5.3	Biological Effects of OH ⁻	67
2.6	Concluding Remarks	67

Chapter 3	Novel Structure Design for Biodegradable Mg and Its Alloys.....	69
3.1	Introduction	69
3.2	Porous Structure	70
3.3	Composites	74
3.3.1	Calcium Phosphate Salts	74
3.3.2	Bioglasses	78
3.3.3	Metals	79
3.3.4	Others	79
3.4	Ultrafine-Grained Structure	80
3.5	Glassy Structure	83
3.6	Concluding Remarks	85
Chapter 4	Surface Modification Techniques for Biodegradable Mg and Its Alloys.....	87
4.1	Introduction	87
4.2	Mechanical Surface Treatment.....	88
4.3	Physical Surface Treatment	91
4.3.1	Plasma Surface Treatment.....	92
4.3.1.1	Low Temperature/Pressure Plasma Surface Treatment.....	92
4.3.1.2	Plasma Spray.....	99
4.3.2	Laser Surface Treatment	101
4.3.2.1	Laser Polishing and Roughening.....	101
4.3.2.2	Laser Surface Melting	103
4.3.2.3	Laser Surface Cladding	103
4.4	Chemical Surface Treatment.....	104
4.4.1	Chemical Conversion Coating.....	104
4.4.1.1	Fluoride Conversion Coating.....	104
4.4.1.2	Alkali Treatment.....	107
4.4.1.3	Hydrothermal Treatment	109
4.4.2	Electrochemical Treatment	113
4.4.2.1	Anodic Oxidation and Micro-Arc Oxidation	113
4.4.2.2	Electrodeposition	121
4.4.2.3	Electrophoretic Deposition	124
4.4.3	Biomimetic Deposition.....	124
4.4.4	Sol-Gel Treatment	129
4.4.5	Organic and Polymer Coating	132
4.4.6	Molecular Self-Assembled Coating.....	136
4.5	Concluding Remarks	141
4.5.1	Coating Roughness.....	141
4.5.2	Adhesion.....	141
4.5.3	Long-Term Corrosion Behavior.....	141
4.5.4	Biocompatibility	142

Chapter 5	Mg with High Purity for Biomedical Applications.....	143
5.1	Introduction	143
5.1.1	Commercial Pure Mg (CP-Mg).....	143
5.1.2	High-Purity Mg (HP-Mg)	144
5.1.3	Previous Studies on Pure Mg for Industrial/ Engineering Applications.....	145
5.2	Development of Pure Mg as Degradable Metallic Biomaterial	147
5.2.1	Impurities	148
5.2.1.1	Fe	148
5.2.1.2	Ni	149
5.2.1.3	Cu.....	149
5.2.1.4	Co.....	150
5.2.2	Fabrication, Hot and Cold Working, and Heat Treatment.....	150
5.2.3	Microstructure and Mechanical Properties.....	152
5.2.4	Degradation in Simulated Body Fluids	153
5.2.5	Cytotoxicity	159
5.2.6	Hemocompatibility	161
5.2.7	Antibacterial Properties	161
5.2.8	In Vivo Performance in Animal Models.....	162
5.3	New Advances in Property Improvements on Pure Mg for Medical Purposes.....	163
5.3.1	New Techniques for Enhancing Mechanical Properties	163
5.3.2	New Methods for Enhancing Corrosion Resistance	165
5.3.3	New Ways for Enhancing Biocompatibility	168
5.4	Concluding Remarks	170
Chapter 6	Mg-Ca-Based Alloy Systems for Biomedical Applications	173
6.1	Introduction	173
6.1.1	Calcium	173
6.1.2	Previous Studies on Mg-Ca Alloy Systems for Engineering Applications	173
6.2	Development of Mg-Ca Binary Alloys as Degradable Metallic Biomaterials	174
6.2.1	Alloy Composition Design	174
6.2.2	Fabrication, Hot and Cold Working, and Heat Treatment.....	174
6.2.2.1	Metallurgy Method	174
6.2.2.2	Powder Metallurgy Method	175
6.2.2.3	Hot and Cold Working.....	175

6.2.3	Microstructure and Mechanical Properties.....	175
6.2.3.1	Microstructure	175
6.2.3.2	Mechanical Properties	177
6.2.4	Degradation in Simulated Body Fluids.....	177
6.2.5	Cytotoxicity and Hemocompatibility	181
6.2.6	In Vivo Performance in Animal Models.....	181
6.3	Development of Mg–Ca–X Ternary Alloys as Degradable Metallic Biomaterials	185
6.3.1	Alloy Composition Design	185
6.3.2	Fabrication, Hot and Cold Working, and Heat Treatment.....	186
6.3.2.1	Mg–Ca–Zn Alloys.....	186
6.3.2.2	Mg–Ca–Zr Alloys	187
6.3.2.3	Mg–Ca–Li Alloys.....	187
6.3.2.4	Mg–Ca–Sr Alloys.....	187
6.3.2.5	Other Ternary Mg–Ca–X Alloys.....	188
6.3.3	Microstructure	188
6.3.3.1	Mg–Ca–Zn Alloys.....	188
6.3.3.2	Mg–Ca–Zr Alloys	189
6.3.3.3	Mg–Ca–Li Alloys.....	190
6.3.3.4	Mg–Ca–Sr Alloys.....	191
6.3.3.5	Mg–Ca–Mn Alloys.....	191
6.3.3.6	Mg–Ca–Sn Alloys	192
6.3.3.7	Mg–Ca–Bi Alloys	193
6.3.3.8	Mg–Ca–Si Alloys	193
6.3.4	Mechanical Properties.....	193
6.3.4.1	Mg–Ca–Zn Alloys.....	193
6.3.4.2	Mg–Ca–Zr Alloys	196
6.3.4.3	Mg–Ca–Li Alloys.....	196
6.3.4.4	Mg–Ca–Si Alloys	196
6.3.4.5	Mg–Ca–Sr Alloys.....	196
6.3.4.6	Mg–Ca–Sn Alloys	197
6.3.5	Degradation in Simulated Body Fluids.....	197
6.3.6	Cytotoxicity and Hemocompatibility	201
6.3.7	In Vivo Performance in Animal Models.....	201
6.4	Development of Mg–Ca Quaternary and Multielementary Alloys as Degradable Metallic Biomaterials.....	204
6.4.1	Alloy Composition Design	204
6.4.2	Fabrication, Hot and Cold Working, and Heat Treatment.....	204
6.4.3	Microstructure and Mechanical Properties.....	204
6.4.4	Degradation in Simulated Body Fluids	206
6.4.5	Cytotoxicity and Hemocompatibility	208
6.4.6	In Vivo Performance in Animal Models.....	209

6.5	Concluding Remarks	209
6.5.1	Alloy Composition Design	210
6.5.2	Enhancing Mechanical Properties	210
6.5.3	Enhancing Corrosion Resistance	210
6.5.4	Enhancing Biocompatibility.....	211
Chapter 7	Mg-Zn-Based Alloy Systems for Biomedical Applications	213
7.1	Introduction	213
7.1.1	Zinc.....	213
7.1.2	Previous Studies on Mg-Zn Alloy Systems for Engineering Applications	213
7.2	Development of Mg-Zn Binary Alloys as Degradable Metallic Biomaterials	214
7.2.1	Alloy Composition Design	214
7.2.2	Fabrication, Hot and Cold Working, and Heat Treatment.....	215
7.2.3	Microstructure and Mechanical Properties.....	216
7.2.3.1	Microstructure	216
7.2.3.2	Mechanical Properties	217
7.2.4	Degradation in Simulated Body Fluids.....	219
7.2.5	Cytotoxicity and Hemocompatibility	221
7.2.6	In Vivo Performance in Animal Models.....	221
7.3	Development of Mg-Zn Ternary Alloys as Degradable Metallic Biomaterials	224
7.3.1	Alloy Composition Design	224
7.3.2	Fabrication, Hot and Cold Working, and Heat Treatment.....	225
7.3.2.1	Mg-Zn-Ca Alloys.....	225
7.3.2.2	Mg-Zn-Zr Alloys.....	225
7.3.2.3	Mg-Zn-Y Alloys.....	225
7.3.2.4	Mg-Zn-Mn Alloys.....	226
7.3.2.5	Other Mg-Zn-X Alloys	226
7.3.3	Microstructure and Mechanical Properties.....	226
7.3.3.1	Mg-Zn-Ca Alloys.....	226
7.3.3.2	Mg-Zn-Zr Alloys.....	227
7.3.3.3	Mg-Zn-Y Alloys.....	228
7.3.3.4	Mg-Zn-Mn Alloys.....	229
7.3.3.5	Other Mg-Zn-Based Ternary Alloys.....	229
7.3.4	Degradation in Simulated Body Fluids	232
7.3.4.1	Mg-Zn-Ca Alloys.....	232
7.3.4.2	Mg-Zn-Zr Alloys.....	235
7.3.4.3	Mg-Zn-Y Alloys.....	235
7.3.4.4	Mg-Zn-Mn Alloys.....	236
7.3.5	Cytotoxicity and Hemocompatibility	236
7.3.6	In Vivo Performance in Animal Models.....	239

7.4	Development of Mg-Zn Quaternary Alloys as Degradable Metallic Biomaterials	240
7.4.1	Alloy Composition Design	240
7.4.2	Fabrication, Hot and Cold Working, and Heat Treatment.....	240
7.4.3	Microstructure and Mechanical Properties.....	241
7.4.4	Degradation in Simulated Body Fluids.....	243
7.4.5	Cytotoxicity and Hemocompatibility	245
7.5	Concluding Remarks	246
7.5.1	Alloy Composition Design	246
7.5.2	Enhancing Mechanical Properties	246
7.5.3	Enhancing Corrosion Resistance	247
7.5.4	Enhancing Biocompatibility.....	247
Chapter 8	Mg-Sr-Based Alloy Systems for Biomedical Applications	249
8.1	Introduction	249
8.1.1	Strontium.....	249
8.1.2	Previous Studies on Mg-Sr Alloy Systems for Engineering Applications	249
8.2	Development of Mg-Sr Binary Alloys as Degradable Metallic Biomaterials	250
8.2.1	Alloy Composition Design	250
8.2.2	Fabrication, Hot and Cold Working, and Heat Treatment.....	250
8.2.3	Microstructure and Mechanical Properties.....	251
8.2.3.1	Microstructure	251
8.2.3.2	Mechanical Properties	252
8.2.4	Degradation in Simulated Body Fluids.....	252
8.2.5	Cytotoxicity and Hemocompatibility	254
8.2.6	In Vivo Performance in Animal Models.....	254
8.3	Development of Mg-Sr Ternary Alloys as Degradable Metallic Biomaterials	255
8.3.1	Alloy Composition Design	255
8.3.2	Fabrication, Hot and Cold Working, and Heat Treatment.....	256
8.3.3	Microstructure and Mechanical Properties.....	256
8.3.3.1	Microstructure of the Mg-Sr-Based Ternary Alloys	256
8.3.3.2	Mechanical Properties of Mg-Sr-Based Ternary Alloys	259
8.3.4	Degradation in Simulated Body Fluids.....	260
8.3.5	Cytotoxicity and Hemocompatibility	261
8.3.6	In Vivo Performance in Animal Models.....	262

8.4	Development of Mg-Sr Quaternary Alloys as Degradable Metallic Biomaterials	262
8.4.1	Alloy Composition Design	262
8.4.2	Fabrication, Hot and Cold Working, and Heat Treatment.....	263
8.4.3	Microstructure and Mechanical Properties.....	263
8.4.3.1	Microstructure	263
8.4.3.2	Mechanical Properties.....	265
8.4.4	Degradation in Simulated Body Fluids.....	265
8.5	Concluding Remarks	266
8.5.1	Enhancing Mechanical Properties	266
8.5.2	Enhancing Corrosion Resistance	266
8.5.3	Enhancing Biocompatibility.....	267
Chapter 9	Mg-Ag-Based Alloy Systems for Biomedical Applications	269
9.1	Introduction	269
9.1.1	Silver.....	269
9.1.2	Previous Studies on Mg-Ag Alloy Systems for Engineering Applications	270
9.2	Development of Mg-Ag Binary Alloys as Degradable Metallic Biomaterials	270
9.2.1	Alloy Composition Design	270
9.2.2	Microstructure and Mechanical Properties.....	271
9.2.3	Degradation in Simulated Body Fluids	273
9.2.4	Cytotoxicity and Hemocompatibility	273
9.2.5	Antibacterial Property	274
9.3	Development of Mg-Ag-Based Alloys as Degradable Metallic Biomaterials	274
9.3.1	Mg-Zn-Ag Alloy System as Degradable Biomaterials	274
9.3.1.1	Alloy Composition Design	274
9.3.1.2	Microstructure and Mechanical Properties	275
9.3.1.3	Degradation in Simulated Body Fluids	276
9.3.1.4	Cytotoxicity and Hemocompatibility	277
9.3.1.5	Antibacterial Property	278
9.3.2	Mg-Nd-Zn-Ag-Zr Alloy System as Degradable Biomaterial	278
9.3.2.1	Microstructure and Mechanical Properties	278
9.3.2.2	Degradation in Simulated Body Fluids	278
9.4	Possible Methods of Property Improvement for Mg-Ag-Based Alloy Systems.....	280
9.4.1	Current Techniques for Enhancing Mechanical Properties	280