NATURAL AND SYNTHETIC BIOMEDICAL POLYMERS

Edited by

SANGAMESH G. KUMBAR, PhD.
CATO T. LAURENCIN, M.D., PhD.
MENG DENG, PhD.

Natural and Synthetic Biomedical Polymers

Natural and Synthetic Biomedical Polymers

Edited By
Sangamesh G. Kumbar
Cato T. Laurencin
Meng Deng

ELSEVIER
AMSTERDAM • BOSTON • HEIDELBERG • LONDON • NEW YORK • OXFORD
PARIS • SAN DIEGO • SAN FRANCISCO • SINGAPORE • SYDNEY • TOKYO

Elsevier
30 Corporate Drive, Suite 400, Burlington, MA 01803, USA
525 B Street, Suite 1800, San Diego, CA 92101-4495, USA

First edition **2014**

Library of Congress Cataloging-in-Publication Data
Natural and synthetic biomedical polymers/edited by Sangamesh Kumbar, Cato Laurencin, Meng Deng. — First edition.
pages cm
Summary: "Polymer scientists have made an extensive research for the development of biodegradable polymers which could find enormous applications in the area of medical science. Today, various biopolymers have been prepared and utilized in different biomedical applications. Despite the apparent proliferation of biopolymers in medical science, the Science and Technology of biopolymers is still in its early stages of development. Tremendous opportunities exist and will continue to exist for the penetration of biopolymers in every facet of medical science through intensive Research and Development. Therefore, this chapter addresses different polymerization methods and techniques employed for the preparation of biopolymers. An emphasis is given to cover the general properties of biopolymers, synthetic protocols and their biomedical applications. In order to make the useful biomedical devices from the polymers to meet the demands of medical science, various processing techniques employed for the development of devices have been discussed. Further, perspectives in this field have been highlighted and at the end arrived at the conclusions. The relevant literature was collected from different sources including Google sites, books and reviews"— Provided by publisher.
Includes bibliographical references and index.
ISBN 978-0-12-396983-5 (hardback)
1. Biopolymers. 2. Biodegradable plastics. I. Kumbar, Sangamesh, editor of compilation. II. Laurencin, Cato, editor of compilation. III. Deng, Meng, editor of compilation.
TP248.65.P62N38 2014
610.28—dc23 2014000085

British Library Cataloguing in Publication Data
A catalogue record for this book is available from the British Library

For information on all **Elsevier** publications
visit our web site at store.elsevier.com

Printed and bound in USA
14 15 16 17 18 10 9 8 7 6 5 4 3 2 1

ISBN: 978-0-12-396983-5

Dedication

Sangamesh G. Kumbar—To my parents (Mr. and Mrs. G. B. Kumbar), wife Swetha, and daughter Gauri.

Cato T. Laurencin—To my wife Cynthia, and my children Ti, Michaela, and Victoria.

Contributors

Aja Aravamudhan *Department of Orthopaedic Surgery, Institute for Regenerative Engineering, Raymond and Beverly Sackler Center for Biomedical, Biological, Physical and Engineering Sciences, The University of Connecticut, Farmington, CT, USA*

Brittany L. Banik *Department of Bioengineering, The Pennsylvania State University, PA, USA*

Mark R. Battig *Department of Bioengineering, College of Engineering, The Pennsylvania State University, PA, USA*

Steve Brocchini *UCL School of Pharmacy, University College London, London, UK*

Justin L. Brown *Department of Bioengineering, The Pennsylvania State University, PA, USA*

Karen Burg *Institute for Biological Interfaces of Engineering, Clemson, USA*

Diane J. Burgess *Department of Pharmaceutical Sciences, School of Pharmacy, University of Connecticut, Storrs, CT, USA*

Sheiliza Carmali *UCL School of Pharmacy, University College London, London, UK*

Tram T. Dang *Center for Biomedical Engineering, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA*

David H. Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology, Cambridge, MA, USA

Meng Deng *Department of Orthopaedic Surgery, Institute for Regenerative Engineering, Raymond and Beverly Sackler Center for Biomedical, Biological, Physical and Engineering Sciences, The University of Connecticut, Farmington, CT, USA*

Abraham (Avi) Domb *School of Pharmacy-Faculty of Medicine, The Hebrew University of Jerusalem, Jerusalem, ISR*

Lakshmi Sailaja Duvvuri *Department of Pharmaceutics, National Institute of Pharmaceutical Education and Research, Hyderabad, India*

Muntimadugu Eameema *Department of Pharmaceutics, National Institute of Pharmaceutical Education and Research, Hyderabad, India*

Jennifer Elisseeff *Johns Hopkins School of Medicine, Translational Tissue Engineering Center, Wilmer Eye Institute and Department of Biomedical Engineering, Baltimore, MD, USA*

Sahar E. Fard *Department of Chemistry, Chemical Biology, and Biomedical Engineering, Stevens Institute of Technology, Hoboken, NJ, USA*

Bing Gu *Department of Pharmaceutical Sciences, School of Pharmacy, University of Connecticut, Storrs, CT, USA*

Jinshan Guo *Department of Bioengineering, Materials Research Institute, The Huck Institute of The Life sciences, The Pennsylvania State University, PA, USA*

Umesh Gupta *Department of Pharmaceutical Sciences, College of Pharmacy, South Dakota State University, Brookings, SD, USA*

Matthew D. Harmon *Department of Orthopaedic Surgery, Department of Material Science and Engineering, Institute for Regenerative Engineering, Raymond and Beverly Sackler Center for Biomedical, Biological, Physical and Engineering Sciences, The University of Connecticut, Farmington, CT, USA*

Markus Heiny *Institute for Macromolecular Chemistry, University of Freiburg, Freiburg, Germany*

Anjana Jain *Biomedical Engineering Department, Worcester Polytechnic Institute, Worcester, MA, USA*

Roshan James *Department of Orthopaedic Surgery, Institute for Regenerative Engineering, Raymond and Beverly Sackler Center for Biomedical, Biological, Physical and Engineering Sciences, The University of Connecticut, Farmington, CT, USA*

Tao Jiang *Department of Medicine, Institute for Regenerative Engineering, Raymond and Beverly Sackler Center for Biomedical, Biological, Physical and Engineering Sciences, The University of Connecticut, Farmington, CT, USA*

Ravindra R. Kamble *Department of Studies in Chemistry, Karnatak University, Dharwad, Karnataka, India*

Lohitash Karumbaiah *Department of Biomedical Engineering, Georgia Institute of Technology, Atlanta, Georgia, USA*

Ali Khademhosseini *Center for Biomedical Engineering, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA*

Harvard-MIT Division of Health Sciences and Technology, Massachusetts Institute of Technology, Cambridge, MA, USA

Wyss Institute for Biologically Inspired Engineering, Harvard University, Boston, MA, USA

Wahid Khan *Department of Pharmaceutics, National Institute of Pharmaceutical Education and Research, Hyderabad, India*

School of Pharmacy-Faculty of Medicine, The Hebrew University of Jerusalem, Jerusalem, ISR

Sangamesh G. Kumbar *Department of Orthopaedic Surgery, Department of Material Science and Engineering, Department of Biomedical Engineering, Institute for Regenerative Engineering, Raymond and Beverly Sackler Center for Biomedical, Biological, Physical and Engineering Sciences, The University of Connecticut, Farmington, CT, USA*

Cato T. Laurencin *University Professor, Albert and Wilda Van Dusen Distinguished Professor of Orthopaedic Surgery, Professor of Chemical, Materials and Biomolecular Engineering; Chief Executive Officer, Connecticut Institute for Clinical and Translational Science; Director, The Raymond and Beverly Sackler Center for Biomedical, Biological, Engineering and Physical Sciences; Director, Institute for Regenerative Engineering, The University of Connecticut, Farmington, CT, USA*

Paul Lee *Department of Chemistry, Chemical Biology, and Biomedical Engineering, Stevens Institute of Technology, Hoboken, NJ, USA*

Adnan Memic *Center for Biomedical Engineering, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA*

Harvard-MIT Division of Health Sciences and Technology, Massachusetts Institute of Technology, Cambridge, MA, USA

Center of Nanotechnology, King Abdulaziz University, Jeddah, Saudi Arabia

Sara K. Murase *Departament d'Enginyeria Química, Universitat Politècnica de Catalunya, Barcelona, ESP*

Ahmed A. Nada *Department of Orthopaedic Surgery, Institute for Regenerative Engineering, Raymond and Beverly Sackler Center for Biomedical, Biological, Physical and Engineering Sciences, The University of Connecticut, Farmington, CT, USA*

Rajaram K. Nagarale *Department of Chemical Engineering, Indian Institute of Technology Kanpur, Uttar Pradesh, India*

Dianna Y. Nguyen *Department of Bioengineering, Materials Research Institute, The Huck Institute of The Life sciences, The Pennsylvania State University, PA, USA*

Mehdi Nikkhah *Center for Biomedical Engineering, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA*

Harvard-MIT Division of Health Sciences and Technology, Massachusetts Institute of Technology, Cambridge, MA, USA

Meera Parthasarathy *School of Chemical & Biotechnology, SASTRA University, Centre for Nanotechnology & Advanced Biomaterials, Thanjavur, Tamil nadu, India*

Omathanu Perumal *Department of Pharmaceutical Sciences, College of Pharmacy, South Dakota State University, Brookings, SD, USA*

Jordi Puiggalí *Departament d'Enginyeria Química, Universitat Politècnica de Catalunya, Barcelona, ESP*

Walid P. Qaqish *Department of Biomedical Engineering, The University of Akron, Akron, Ohio, USA*

Daisy M. Ramos *Department of Orthopaedic Surgery, Department of Material Science and Engineering, Institute for Regenerative Engineering, Raymond and Beverly Sackler Center for Biomedical, Biological, Physical and Engineering Sciences, The University of Connecticut, Farmington, CT, USA*

Department of Chemical, Materials and Biomedical Engineering, University of Connecticut, CT, USA

Dina Rassias *Biomedical Engineering Department, Worcester Polytechnic Institute, Worcester, MA, USA*

Tarun Saxena *Department of Biomedical Engineering, Georgia Institute of Technology, Atlanta, Georgia, USA*

Swaminathan Sethuraman *Centre for Nanotechnology & Advanced Biomaterials, School of Chemical & Biotechnology, Sastra University, Thanjavur, India*

Kush N. Shah *Department of Biomedical Engineering, The University of Akron, Akron, Ohio, USA*

Venkatram Prasad Shastri *Hermann Staudinger Haus, University of Freiburg, Freiburg, DEU*

Namdev B. Shelke *Department of Orthopaedic Surgery, Institute for Regenerative Engineering, Raymond and Beverly Sackler Center for Biomedical, Biological, Physical and Engineering Sciences, The University of Connecticut, Farmington, CT, USA*

Anuradha Subramaniam *Centre for Nanotechnology & Advanced Biomaterials, Sastra University, Thanjavur, India*

Xiaoyan Tang *Department of Orthopaedic Surgery, Department of Material Science and Engineering, Institute for Regenerative Engineering, Raymond and Beverly Sackler Center for Biomedical, Biological, Physical and Engineering Sciences, The University of Connecticut, Farmington, CT, USA*

Shalumon Kottappally Thankappan *Department of Orthopaedic Surgery, Institute for Regenerative Engineering, Raymond and Beverly Sackler Center for Biomedical, Biological, Physical and Engineering Sciences, The University of Connecticut, Farmington, CT, USA*

Katelyn Tran *Department of Chemistry, Chemical Biology, and Biomedical Engineering, Stevens Institute of Technology, Hoboken, NJ, USA*

Richard T. Tran *Department of Bioengineering, Materials Research Institute, The Huck Institute of The Life sciences, The Pennsylvania State University, PA, USA*

Chandra M. Valmikinathan *Global Surgery Group, Johnson and Johnson, Somerville, NJ, USA*

Yong Wang *Department of Bioengineering, College of Engineering, The Pennsylvania State University, PA, USA*

Iwen Wu *Department of Biomedical Engineering, Johns Hopkins University; Translational Tissue Engineering Center, Wilmer Eye Institute*

Jonathan Johannes Wurth *Institute for Macromolecular Chemistry, University of Freiburg, Freiburg, Germany; BIOSS – Centre for Biological Signalling Studies, University of Freiburg, Freiburg, Germany*

Zhiwei Xie *Department of Bioengineering, Materials Research Institute, The Huck Institute of The Life sciences, The Pennsylvania State University, PA, USA*

Jian Yang *Department of Bioengineering, Materials Research Institute, The Huck Institute of The Life sciences, The Pennsylvania State University, PA, USA*

Yuan Yin *Biomedical Engineering Department, Worcester Polytechnic Institute, Worcester, MA, USA*

Xiaojun Yu *Department of Chemistry, Chemical Biology, and Biomedical Engineering, Stevens Institute of Technology, Hoboken, NJ, USA*

Yang H. Yun *Dept. of Biomedical Engineering, University of Akron, Akron, OH, USA*

Foreword

I am truly delighted to write the foreword for *Natural and Synthetic Biomedical Polymers* edited by well-established leaders and pioneers in the field, Professors Dr. Kumbar, Dr. Laurencin, and Dr. Deng. This book should prove extremely useful as a reference source for all those working in the fields of polymer chemistry and physics, biomaterial science, tissue engineering, drug delivery, and regenerative medicine. Polymeric materials are routinely used in clinical applications, ranging from surgical sutures to drug-eluting devices to implants. In particular, implants and drug delivery devices fabricated using biodegradable polymers provide the significant advantage of being degraded and/or resorbed after they have served their function. Yet, biomedical polymers must satisfy several design criteria, including physical, chemical, biomechanical, biological, and degradation properties when serving as an active implant material. Several natural and synthetic degradable polymers have been developed and are used clinically today. However, a wide range of new polymers, as well as modifications to existing polymers, are constantly being developed and applied to meet on-going and evolving challenges in biomedical applications. For example, polymeric nanostructures, implants, scaffolds, and drug delivery devices are allowing unprecedented manipulation of cell-biomaterial interactions, promotion of tissue regeneration, targeting of therapies, and combined diagnostic and imaging modalities.

This timely book provides a well-rounded and articulate summary of the present status of natural and synthetic biomedical polymers, their structure and property relationships, and their biomedical applications including regenerative engineering and drug delivery. Polymers that are both synthetic and natural in origin have been widely used as biomaterials for a variety of biomedical applications and greatly impacted the advancement of modern medicine. In this regard, 23 concise and comprehensive chapters are prepared by experts in their fields from different parts of the world. The chapters encompass numerous topics that appear prominently in the modern biomaterials literature and cover a wide range of traditional synthetic, natural, and semi-synthetic polymers and their applications. In my opinion, this book presents an excellent overview of the subject that will appeal to a broad audience and will serve as a valuable resource to those working in the fields of polymer science, tissue engineering, regenerative medicine, or drug delivery. I believe that this textbook will be a welcome addition to personal collections, libraries, and classrooms throughout the world.

Kristi S. Anseth
Professor, Department of Chemical and Biological Engineering, University of Colorado

Chapter 1

Polymer Synthesis and Processing

Mahadevappa Y. Karidurаganavar[*], Arjumand A. Kittur[†], Ravindra R. Kamble[*]

[*]*Department of Studies in Chemistry, Karnatak University, Dharwad, India*

[†]*Department of Chemistry, SDM College of Engineering & Technology, Dharwad, India*

Chapter Outline

1.1 INTRODUCTION

Polymers are the most versatile class of biomaterials, being extensively used in biomedical applications such as contact lenses, pharmaceutical vehicles, implantation, artificial organs, tissue engineering, medical devices, prostheses, and dental materials [1–3]. This is all due to the unique properties of polymers that created an entirely new concept when originally proposed as biomaterials. For the first time, a material performing a structural application was designed to be completely resorbed and become weaker over time. This concept was applied for the first time with catgut sutures successfully and, later, with arguable results, on bone fixation, ligament augmentation, plates, and pins [4,5].

Current research on new and improved biodegradable polymers is focused on more sophisticated biomedical applications to solve the patients' problems with higher efficacy and least possible pains. One example is *tissue engineering*, wherein biodegradable scaffolds seeded with an appropriate cell type provide a substitute for damaged human tissue while the natural process of regeneration is completed [6,7]. Another important application of biodegradable polymer